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MOLECULAR ORBITAL CALCULATIONS OF THE TAUTOMERISM OF SOME 1,3-THIAZOLE DRIVATIVES

BY

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B. Sc. In Chemistry
1420 A.H

A THESIS
SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE
OF
MASTER OF SCIENCE IN CHEMISTRY
(M.SC)

UNDER SUPERVION OF

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قال الله عز وجل في كتابه الكريم:

﴿ .. وَمَا أُوتِيتُم مِّنَ الْعِلْمِ إِلَّا قَلِيلاً ﴾

(سورة الإسراء / ٩٠٢)

قال سيدنا رسول الله محمد صلى الله عليه وسلم:

﴿من سلك طريقاً يطلب فيه علماً سلك الله به طريقاً من طرق الجنة وإن الملائكة لتضع أجنحتها رضاً لطالب العلم﴾

(أخرجه أبو داوود)

جامعة أم القرى
كلية العلوم التطبيقية
قسم الكيمياء

استخدام طريقة حسابات المدارات الجزيئية لدراسة عملية التأرجح و التشكل لبعض مشتقات مركب (١،٣)-ثيازول

رسالة مقدمة من

أروى واصل حامد الحربي
بكالوريوس في الكيمياء
١٤٢٠هـ

وذلك كجزء من المتطلبات للحصول على درجة
الماجستير في الكيمياء
(كيمياء فيزيائية)

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١٤٢٧هـ

ACKNOWLEDGEMENT

ACKNOLEDGMENT

In the Name of Allah, Most Gracious, Most Merciful

Glorification for Allah, The Cherisher an Sustainer of the worlds, and may Peace and Blessing be upon Messenger Muhammad, the seal of the prophets and on his household and all of his companion.

All praise is due to Allah and his servant our Master Muhammad for his grace and I ask him to increase my knowledge as well as I can.

I would like to express my thankfulness to the supervisor Dr. Adel A. Mohamed, the associate Prof. of Physical Chemistry, Department of Chemistry, Umm Al-Qura University, Makkah Al-Mukarramah, for establishing the subject of this thesis, continuous advice with valuable criticism, guidance, encouragement and excellent supervision during all stages of this research.

Also, I wish to express my thanks to the head of Chemistry Department Prof. Abdulhadi M. Summan Al-Omary, Professor of Analytical Chemistry, Faculty of Applied Sciences, Umm Al-Qura University, Makkah Al-Mukarramah for his encouragement, care and facilitate all obstructs during my Master research work.

I wish to express my thanks to all colleagues and students at the Department of Chemistry.

A special thanks and gratitude for my brother Dr. Ahmed Al-Harby, Medical resident, Department of Internal Medicine, Royal Victoria Hospital, McGill University, Canada, for helping to get important researches which supported my research.

I dedicate my work to my Father and Mother, my dear husband, sisters, brothers, and my lovely Children.
I would like to express my deep thanks for them, because without their love, encouragement, consolation and patience, this work would not have been possible.

I particularly wish to thank my dear husband for his devotion, patience, and understanding through this study.

Finally, I extended my respect and thanks for my relatives and every body who helped me directly or indirectly through this study. Thanks to Allah at the end as well as it was in the beginning.

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The amino $\rightleftharpoons$ imino tautomerization of the three amino thiazoles and some of their derivatives in gas, water, and CCl_4 phases have been studied using the methods RHF, B3LYP, and MP2 with different basis sets. Both of B3LYP and MP2 levels with 6-311++G(d,p) basis set show that the amino form is the predominant form for 2-, 4- or 5-aminothiazoles.

The process is an endothermic and the contribution of entropy into Gibbs free radical is neglected. The type and position of substituent does not appreciably affect tautomerization process. The NO_2 group substituted on the exocyclic nitrogen atom increases the amount of imino form with equilibrium constant K= 1.109 at B3LYP level.

In case of diaminothiazoles, the imino form **2A5ITH** is found to be the most stable structure in gas phase, while **5I4ATH** is found in solution phase at B3LYP level of calculation, while **3I4ATH** is the highest one in energy. The order of stability of the five structures is; **2A5ITH > 24ATH ≈ 5I4ATH > 3I5ITH > 3I4ATH.** In case of MP2 results, the stability order becomes **24ATH > 2A5ITH > 5I4ATH > 3I5ITH > 3I4ATH**.

In case of the other isomer **25ATH**, both levels show that the diamino form **25ATH** is the most predominant one, while the imino form **3I5ATH** is the least stable form in gas and solution phase.

The effect of type of substituent and its position on the equilibrium position and ratio was investigated using the same levels. In case of **4-** or **5X-2ATH**, the amino form predominancy does not affect by type or position of substituent, but the value of equilibrium constant K decreases, indicating the increase of imino amount. The Gibbs free energy change has the order

$$\mathbf{4CH_3 < 4H < 4NO_2 < 4Cl < 4CHO < 4F}$$

at B3LYP level, while at MP2 level it is

$$\mathbf{4H < 4CH_3 < 4NO_2 < 4Cl < 4F < 4CHO}$$

For 5-position the order of ΔG becomes

$$\mathbf{5CH_3 < 5H < 5F < 5CHO < 5Cl < 5NO_2 \qquad (B3LYP)}$$

$$\mathbf{5CHO < 5NO_2 < 5H < 5CH_3 < 5Cl < 5F \qquad (MP2)}$$

INTRODUCTION

1. INTRODUCTION

Tautomerism, conformational properties, and structures have attracted considerable research interest over many years. Tautomerism is involved in many chemical processes, including condensation reactions and plays a significant role in several processes related to proton transfer and hydrogen bonding.

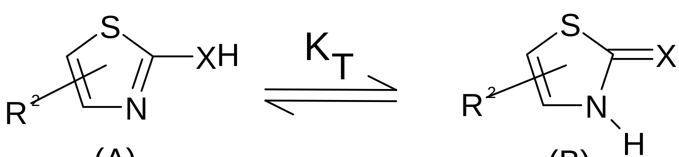
Because of the multiplicity of possible forms, the tautomerism of hydroxy, amino and thiolo heterocycles offers a challenging field of investigation for physical and quantum chemistry. The tautomerism of five membered ring heterocycles appears to be more sensitive to substitution than the six membered rings, because the electronic effects of the substituents bonded to a small-sized cycle on the basicity of the aza nitrogen are stronger than those on a six-membered cycle. Consequently, thiazole derivatives are more suitable as models in investigating the tautomerism of the amino group in heterocyclic series than pyridine amino derivatives(1).

The synthesis of heterocyclic rings containing S and N atoms has been particularly attractive because of their applications in pharmacology(2,3). Many naturally occurring and synthetic thiazole

derivatives exhibit biological activities, such as antibiotic, anti-inflammatory, anthelmintic, or fungicidal properties[4-7].

Owing to its significance in many chemical and biological reactions, the tautomerism of heterocyclic compounds continues to be a matter of intense experimental and theoretical research[8]. Most theoretical and experimental studies have concentrated on the tautomerism of 2-hydroxypyridine, uracil, thymine, cytosine, and pyrazine[9-28]. Solvent effects often play an important role in organic chemistry and many chemical equilibrium may be substantially modified by a change of molecular environment[29].

Thiazole derivatives can exist in many tautomeric forms as illustrated by the following equilibrium.



(A) (B)

(X = NR, O, S)

Several spectroscopic investigations[30], by IR[31-33], X-ray[34,35], UV[36,37] and NMR[38-41] indicate that the most populated form of 2-aminothiazole is the amino aromatic form (A). On the other hand, the introduction of substituents on the thiazole ring does not produce

significant effects on the position of the tautomeric equilibrium[1]. The strong electron withdrawing groups on the exocyclic nitrogen e.g. 2-(p-tosylamino)thiazole shift the position of tautomeric equilibrium toward the imino tautomer, while the same substituents in 5-position prefer the amino tautomer[42].

AIM OF THE WORK

The present work has been performed with an aim to achieve the following goals for 2-amino, 2-hydroxy, and 2-mercapto thiazole tautomers:

(1) Checking the validity of different theoretical methods to study the tautomerism of the above thiazoles.

(2) Obtaining accurate theoretical data of the geometrical structure, relative stability, dipole moment and other ground state properties of each tautomer in gas phase and in apolar and polar solvents by means of the polarizable continuum model PCM.

(3) Studying of the mechanism of 1,3-sigmatropic rearrangement for the transformation between different tautomers, and evaluate the thermodynamic parameters for such reactions e.g. activation energy E_a, heat of reaction ΔH, the Gibbs free energy change ΔG, entropy change ΔS and equilibrium constant K_T .

(4) Exploring the effect of substituents type and position on the tautomerism process.

(5) Investigation of solvent effects on the calculated thermodynamic properties of the tautomers and their prototropic equilibrium.

Literature survey

2. LITERATURE SURVEY

2.1. BIOLOGICAL AND MEDICINAL ACTIVITIES

The biological activity of 2-aminothiazole derivatives as inhibitors of human cancer was studied[43,44]. In addition to its antitumor activity, it was found to be an inhibitor of cyclin-dependent kinase 5/P25 as a potential treatment for Alzheimer's disease[45]. Misra et al.[46] prepared N-aryl-2-aminothiazole and studied its inhibition of **CDK1** / **CDK2**[47] / **CDK4** in vitro.

The biological activities of 2-aminothiazole derivatives on human adenosine receptors were investigated[48]. Medically, 2-aminothiazole and its derivatives have an important role as potent inducible nitric oxide (iNOS) synthase inhibitors, so it is expected that (4R, 5R)-5-ethyl-2-imino-4-methyl-1,3-thiazolidine may be therapeutically useful for the treatment of disease related to excess production of NO[49]. In addition, 2-aminodiazole derivatives have antimicrobial activity[50] against Gram-positive bacteria[51], antifungal activity[52], anaesthetic activity[53], and anti-inflammatory activity[54] and enter in creating antiviral drugs[55]. On the other hand, the activity of benzothiazole derivatives for photosynthesis inhibition in algae chlorella vulgaris and in spinach chloroplasts was correlated with lipophilicity and dipole moments of the effectors using the

Hansch method[56]. Raciti et al.[57] studied the relationship between chemical structure and inhibitory activity of some hydrazine-thiazole derivatives on rat liver mitochondria monoamine oxidase. The photo physical properties of the two thiazole orange derivatives are affected by the interaction with DNA and oligonucleotides[58]. Both photo physical measurements and molecular calculations have been done to assess their possible mode of interaction with DNA. The fluorescence quantum yield when the two derivatives bind with single-stranded oligonucleotides is smaller than that when they bond to double-stranded samples.

2.2. INDUSTRIAL ACTIVITY

Karpov et al.[59] studied the effect of 2-aminothiazole derivatives on the biological resistance corrosion activity of jet fuels under conditions of water condensation. 2-Aminothiazole derivatives are very important compounds in synthesizing methane dyes[60], azodisperse dyes, which are used for dyeing polyester fabrics[61], monoazo disperse dyes, which are strong chromophorically and build up on polyester[62] and bishetaryl monoazo dyes[63]. The light absorption and fluorescence properties of these dyes have been investigated[64].

2.3. TAUTOMERISM AND SPECTROSCOPY

2.3.1. EXPERIMENTAL METHODS

2.3.1.1. *KINETICS*

The amino tautomer is the more active species in the reactions of 2,4-dinitrofluorobenzene with some 2-aminothiazole derivatives in DMSO at 30°C. The kinetics and mechanism of such reactions have been investigated[65]. The H-D exchange kinetics of thiazole in DMSO-d6-CD_3OD containing CD_3ONa, indicated that the C_2 and C_5 positions had nearly identical reactivity and the proton at C_4 did not exchange. The reactivity of C_5 in 2-(N,N-dimethylamino)-thiazole was less than that in thiazole, while the exchange at C_5 in 2-ethoxycarbonylthiazole was too fast to measure. The involvement of tautomeric aminothiazole intermediates in the exchange mechanism with 2-aminothiazole was investigated[66].

2.3.1.2. *pK$_a$ MEASUREMENTS*

pK_{BH^+} values of a number of 2-aminothiazoles, of their methiodides and of some fixed model imines have been measured in water at 25°C. The tautomeric constant K_T is determined. The results showed that 2-aminothiazoles generally exist in the aminoaromatic form and protonated at the aza-nitrogen while 2-p-tosylaminothiazole exists predominantly in the imino form and protonated at the exocyclic nitrogen[67]. A comparison of the pK_a values of 5-substituted aminothiazoles with those of

5-substituted 2-N,N-dimethylaminothiazoles enabled the aromatic amino tautomeric structure to be assigned to 2-aminothiazole derivatives(68).

2.3.1.3. *IR SPECTRA*

An examination of the infrared spectra of 2-aminothiazole was made in the 3 and 4μ region in $CHCl_3$ solution and showed that 2-aminothiazole exists predominantly in the amino form(31). The infrared spectra of anions of deauterated pyridine, quinoline and thiazole series retained the intense band of vibrations of the aromatic heterocycle in the 1530-1600 cm^{-1} range and, in addition, the ND2 band at 1100-1200 cm^{-1}. On the other hand, the intense band of NH_2 at 1590-1650 cm^{-1} was absent, confirming the amino structure of these bases(32). Infrared spectra in the solid state and in different solutions for thiazole, 2-aminothiazole and 2-amino[$^2H_2$]-thiazole, as well as, Raman spectrum of microcrystalline powder for 2-aminothiazole have been investigated. The molecular structure of thiazole has been determined by microwave spectrometry, confirming the generally accepted hypothesis of a planar structure, therefore, the molecule is a planar with C_s point group and the thermodynamic properties were computed(33).

Arenas et al.(69) studied the ν(OH), ν(C:O) bands of thiazole-2-carboxylic acid in solid state and DMSO solutions. He also investigated the NH_2 bands of 2-aminothiazole in solid state and in solutions in inert

and proton-donor solvents. The IR spectra of the acid showed bands in ν(OH) region which arise from O-H...N_c strong intermolecular association, where N_c is the thiazolinic nitrogen atom, and resolved doublets in the ν(C:O) region which arise from rotational isomers. Solutions of 2-aminothiazole showed NH_2 stretching bands corresponding to the free and associated molecules which arise from N-H…N_c intermolecular associations[(69)]. The infrared and ultraviolet absorption spectra and the dissociation constants of 2-aminobenzothiazole and of its 4-, 5-, 6- and 7-Me and MeO derivatives showed that these compounds exist predominatly in the amine form. The substituents do not effect noticeably the position of the absorption maximum in the 3 μ region, nor that of the principal absorption at about 260 mμ of the neutral molecules. The minor absorption bands in acid solution at 270-300 mμ were to be more affected by the substituents. The molecular structure was considered in relation to some aspects of their physicochemical behavior (basicity, ultraviolet and infrared absorption spectrum). The resonance phenomena in these compounds are in general much more affected by presence of electron-donating substituents in the cation than in the neutral molecules[(70)].

IR and Raman spectra of 2-mercaptothiaziole in solid state, CS_2 and in $CHCl_3$ solutions have been studied. The thiocarbonyl form, inter-molecular hydrogen-bonded dimmers in solid state, and unassociated

molecules in dilute solutions of inert solvents have been established[71]. The structural study in the solid state and in the liquid phase and the thiol-thione tautomeric equilibrium study of trifluoromethyl 2-mercapto-1,3-thiadiazole derivatives were investigated. Vibrational spectra were calculated for both tautomers and compared with experimental data. The experimental and theoretical results can be interpreted in terms of the existence of a thione tautomer in the solid and in solution[72].

The IR spectra (in solid, liquid, and solution) and Raman spectra in solid state of Δ-4-thiazoline-2-thione and its N-deutero homolog were investigated[73]. Polarization IR spectra of 2-mercaptothiazoline and 2-mercapto-1-methylimidazole were measured in the frequency ranges of the $\nu_{N\text{-}H}$ and $\nu_{N\text{-}D}$ bands at 77 and 298K. The spectra were attributed to cyclic N-H…S hydrogen-bond dimers, which are present as structural units in the lattices. The influence of the electronic properties of the associating small-ring molecules on the spectral properties of the hydrogen bonds was also investigated[74].

2.3.1.4. *UV SPECTRA*

Sheinker et al.[36] studied the infrared and ultraviolet spectra of thiazole, methylthiazole, 2-aminothiazole, and 2-iminothiazolines. The data show that in the crystalline state and in solutions, 2-aminothiazole and its derivatives have the amino structure. 2-Aminothiazole, its 4-Me and

their N-Ac derivatives and 2-(methylacetamido)-4-methylthiazole exist as the thiazole tautomers, according to their IR and UV spectra[37].

Data for the ultraviolet light absorption given by Cook for 5-amino-2-mercaptothiazoles show the importance of the substituents in the 4-position of the thiazole nucleus for the tautomer form. If the substituent is H or an alkyl group, the thiol form is present in alkaline solution, while in alcoholic solution the thione form is present. But if substituent in the 4-position has a great conjugating power, such as Ph group, the thiol form is also present in neutral solution[75]. Investigation of the infrared and ultraviolet absorption spectra of the derivatives of thiazole showed that the 2-hydroxy and 2-mercaptothiazoles exist in the crystalline state and in solution in the form of oxo and thionic structure, respectively[76]. The UV spectra of thiazoline-2-thione, thiazolidine-2-thione, benzothiazoline-2-thione, 3-methylbenzothiazoline-2-thione and 2-methylthiobenzothiazole in arrange of solvents have been detected[77].

The 5-Me group of 2-(methylthio)thiazole increases the rate of quaternization by MeI, while the rate of formation of thiazoliumiodides from the 4-thiazoline-2-thiones is increased by the introduction of a 4-Me or 5-Me group. The position of the UV absorption bands are in agreement with calculated electronic transition energies for these compounds[78]. The IR and UV spectra of some tetrahydro-2-thiothiazines and –thiazoles are

compared with those of 4-hydroxy substituted compounds. The position of the O-H stretching, O-H deformation, and C-O stretching bands of tetrahydro-2-thiazoles were investigated. The UV spectra of these compounds and derived dihydro-2-thiothiazines and -thiazoles were compared with those of certain 2- and 3-substituted derivatives. Compounds capable of thione-thiol tautomerism exist as the thione form in aqueous solution[(79)].

2.3.1.5. *X-RAY SPECTRA*

Crystals of 2-amino-1,3-thiazole are orthorhombic, space group pbca, with eight molecules in the unit cell. Conformational parameters are calculated and compared to those of similar molecules. The exocyclic nitrogen atom, slightly out of the thiazole ring plane, is linked by hydrogen bonds to two endocyclic N atoms of two symmetry-related molecules[(34)].

Toplak et al.[(35)] studied the geometries of the two crystallographically molecules (2-aminothiazoles and 2-aminothiazolinone). The crystal structures of both compounds contain two types of intermolecular hydrogen bonds. X-ray analysis establishes that 4-(3-nitrophenyl)thiazole-2(3H)-thione exists in the solid state as the thione tautomer[(80)].

2.3.1.6. *NMR SPECTRA*

Forlani et al.[38] measured the ^{1}HNMR of several 2,4-diamino-thiazoles in DMSO and found that hydrohalide salts of aminothiazole derivatives are present in the imino form. On the other hand, the ^{1}HNMR of 2-aminothiazoles derivatives in $(CD_3)_2SO$ were studied. A distinction between tautomeric forms of 2-aminothiazole is possible from a comparison with fixed models on the amino and imino forms. The imino form predominates only when the SO_2Ar group is bonded to the exocyclic nitrogen atom. In all other cases, the amino form is prevalent. The electronic effects of substituents bonded to C_4 and C_5 of the thiazole ring on the ζ values of the NH_2 group in position two were investigated[42]. ^{1}H and ^{13}C NMR chemical shifts and coupling constants of 2-aminothiazoles and 2-iminothiazolines were studied in terms of tautomerism between amino and imino forms[39].

Tóth et al.[40] studied the amino $\rightleftharpoons$ imino tautomerism of 2-aminothiazoles and their salts. It has been established that in the acid-catalyzed nitramin rearrangement of 2-nitroaminothiazoles the second protonation of the compounds protonated at the exo-nitrogen atom in concentrated sulphuric acid initiates the cleavage of the nitro group.

[5,5]Sigmatropic shift of N-phenyl-N`-(2-thiazolyl) hydrazines and N,N`-bis(2-thiazolyl)hydrazines in acid-catalyzed benzidine-type rearrangement into 2-amino-5(p-aminophenyl)thiazole and 5,5`-bis(2-aminothiazole) derivatives were investigated(81). ^{13}C NMR of variously substituted phenylthiazoles (2-Ph, 4-Ph, and 5-Ph) was investigated and the dihedral angle between the Ph and thiazole ring systems was detected. Comparison with other heterocyclic ring systems indicated that the perturbation observed on Ph substitution decreased with increase in heteroatom electronegativity. Steric interactions were observed in 4,5-disubstituted phenylthiazoles and the substituents effects were nonadditive; additivity was observed in 2,4- and 2,5-disubstituted phenylthiazoles. The protonation of 2-Ph, 4-Ph and 5-Ph thiazole and the tautomerization of 5-NH_2, 5-SH and 5-OH-2-phenylthiazoles were studied(82). ^{1}H and ^{13}C NMR chemical shifts, heteronuclear coupling constants, spin-lattice relaxation time, and nuclear Overhouser enhancements (NOE) for 2-amino-4(5-furyl)thiazole (ANFT) and its N-formyl analogue N-(4(5-nitro-2-furylthiazole)formamide (FANFT) were investigated. ^{1}H, ^{13}C NMR, and NOEs provide further support for the prevalence of the 2-amino tautomer over the 2-iminiothiazoline tautomer(41).

^{13}C NMR spectra of 18 thiazoles (R=H, Me, Br, Cl, NH_2,...) were recorded. The ^{13}C chemical shifts of thiazole derivatives and thiazolo[2,3-e]tetrazoles were investigated as a function of the nature of the substituent and the electronic structure of the thiazole ring. The 2-azido substitutedthiazoles show azido-tetrazole tautomerism(83). The UV spectra of 4-thiazoline-2-thiones and their 2-alkylthiothiazole isomers, were analyzed for protomeric thiol-thione in molecules in the neutral state, solvent effect, and proton fixation. The NMR spectra showed a thiol-thione equilibrium, effect of substituents and the presence of ionized molecules(84). ^{13}C NMR data for a series of 4-thiazoline-2-thione have been investigated. Substituent chemical shift effects for methyl and phenyl substitution have been studied in comparison with substituent chemical shift effects in other heterocyclic systems. In the parent compound, the thione structure is the major tautomer. The preference for the thione rather than the thiol form in a number of heterocyclic systems was established(85).

2.3.2. THEORETICAL METHODS AND CALCULATIONS

Arriau et al.(86) used the HMO method to calculate energies of 5-membered heterocyclic compounds containing 1 or 2 heteroatoms and OH, SH, amino and alkyl functional groups. The calculated order of relative stabilities of tautomers agrees with experimental. They found that the substituents group Me, NH_2 and SH have a greater effect on the

tautomeric equilibrium than does the heteroatom. These substituents always favor the aromatic tautomeric form, while the OH substituent favors the tautomeric form containing a keto group. The concurrent coordination of N atoms in 2-aminothiazoles was studied by the quantum chemical MNDO method. The validity of the fragmentation model as applied to studying the reaction of protonation of 2-aminothiazoles, taking into account their tautomerism was analyzed and proved[(87)]. In addition, a SCF-MNDO study was made of the equilibrium between the thiol and thione tautomers of four species possessing a five-membered heterocyclic ring, where nitrogen and oxygen or sulfur are α-heteroatoms. The nucleophilicity of each specific site in both forms were discussed in terms of net atomic charges and the HOMO constitution of the molecules[(88)]. The optimum geometries, calculated by a gradient method, were compared with experimental molecular structures and results of calculations applying an empirical force field and a theoretical one (ab initio calculations). The heats of formation, dipole moments, and ionization energies of some of the compounds were calculated[(89)]. The positions of the tautomeric equilibria for a number of thioacyl substituted of 2-aminothiazoles and 2-amino-benzothiazoles were determined by spectroscopy with the use of model compounds. Quantum-chemical calculations by the CNDO/2 method were made for some of thioacyl derivatives of 2-aminothiazole and 2-imino-thiazole compounds[(90)].

Photoelectron spectroscopy and quantum mechanical calculations (STO-3G, CNDO/S and EHT) were used to compare the electronic structures of thiazole and isothiazole. In the case of isothiazole, there is an inversion of the two highest occupied MO's between STO-3G and CNDO/S calculations[(91)]. The bonding modes occurring in five-membered heterocyclic thioketo-compounds were investigated by using the semi-empirical INDO method. In the solid state the thione form of the compounds studied is the dominate one as has been experimentally verified[(92)].

The tautomerism of oxazolidines, thiazolidines and selenazolidines substituted at position two and four by hydroxyl and amino groups was investigated by calculations at HF and MP2 levels, using the 6-311+G(d,p) basis set. The relative stabilities of the tautomers of the heterocycles were calculated in gas phase and in solvents $CHCl_3$ and DMSO utilizing the PCM method. The ab initio calculations, in agreement with the available experimental data, predict that the azolidines substituted at position two and four by a hydroxyl and an amino group exist as amino form in solution, while 2,4-diamino-oxazolidine, –thiazolidine and –selenazolidine occur as mixtures of tautomers. The MP2 calculations gave the best agreement with the experimental data[(93)]. Tahmassebi[(94)] studied the prototropic tautomerism of substituted thiazolidine heterocycles at

B3LYP/6-311+G(2d,p) level. The thermodynamic parameters for the tautomers of heterocycles were calculated in the gas phase and in two different solvent (DMSO and cyclohexane) utilizing IPCM methods. The amino tautomer is the most stable tautomer in all cases, both in gas phase and in solutions[(94)]. An ab initio HF and MP2/6-31G** study of the static polarizabilities of 2,4-substituted imidazoles and thiazoles was investigated. The comparison of the two types of five-membered heterocycles suggests, that the exo cyclic heteroatoms have much more influence upon the calculated hyper-polarizabilities, than the ring heteroatoms[(95)].

The UV photoelectron spectra were reported for isoxazole and 1,3,4-oxadiazole, oxazole and 1,2,5-oxadiazole. The spectra have been assigned on the basis of ab initio calculations, and by comparison with the azoles and thiazoles. Variations in the lone pairs levels at O-, S-, and N- across the azoles, oxazoles, thiazoles, and azines were investigated. It suggested that “through-bond” interactions are more widespread in the azines than previously noted[(96)]. The molecular structure of thiazole has been determined by the joint analysis of data obtained from gas phase electron diffraction (GED), microwave (MW) spectroscopy and ab initio molecular orbital calculations. Vibrational frequency calculations were carried out at the 6-31G(d,p)/SCF and 6-31G(d,p)/MP2 levels. There is an

agreement between the harmonic vibrational frequencies from the 6-31G(d,p)/MP2 force and an experimental IR spectrum[97].

PMR spectra of 9 imidazo[2,1-b]thiazoles were detected. Coupled Hartree-Fock calculations of ring current effects indicated that the main difference in chemical shifts relative to the single ring heterocycles were due to the aromatic character of the imidazothiazole ring system[98]. The preferred tautomeric forms of some 2-oxothiazole derivatives were predicted using acidity constants calculated by experimental and ab initio methods using HF/3-21G and B3LYP/6-31G(d). It was observed that oxo forms were favored. An excellent correlation between experimental and ab initio acidity constant values for non-tautomeric molecules was obtained[99]. ^{14}N and ^{33}S nuclear quadruple coupling constants have been calculated for optimized molecular structures of thiazole. For nitrogen, the B3PW91/6-311+G(df,pd) model was used to calculate of the electric field gradients, and for sulfur, the B3LYP/6-311G(3df,3p) model. The best results are obtained for the B3PW91/6-31G(2d,2pd) optimized molecular structure[100].

Geometry optimizations were performed for both tautomers; thiol and thione of 2-mercapto-1,3-thiadiazoles at both HF and B3LYP levels, with the basis set 3-21G*, 6-31G* and 6-31G**. The theoretical calculations predict that, the thione tautomer to be more stable[72].

Reactions of 2-aminooxazoles and 2-aminothiazoles and their derivatives with dienophiles gave good yields of Diels-Alder adducts[101]. The reactions of 2-(sulfinylamino)thiazole with some dienes under Diels-Alder condition which gave [4+2] Cycloaddition products were investigated[102]. The high regioselectivities observed in the Diels-Alder reactions of thiazole o-Quinodimethane with 2- or 3-bromo-5-hydroxynaphthoquinones were investigated theoretically by ab initio calculations using PM3/3-21G*. The theoretical finding of this study agrees with experimental results and supports the statement that hydrogen bonding plays a crucial role on the regiocontrol of the cycloadditions[103].

Arnaud et al.[104] studied the cyclization of α-iminothioaldehydes into dihydrothiazoles theoretically by ab initio MO theory, that when α-iminothioaldehydes were synthesized by retro-Diels-Alder reaction under flash vacuum thermolysis conditions, they undergo a rearrangement to 2,3-dihydro-1,3-thiazoles which transformed into more stable 2,5-dihydro-1,3-thiazoles.

2.4. MISCELLANEOUS

2.4.1. *PROTON TRANSFER*

Gourriérec et al.[105] synthesized the azoles 2-(2`-hydroxyphenyl)-oxazole (HPO) and 2-(2`-hydroxy phenyl)-4-methylthiazole (HPT) and compared their photo physical behaviour in non-polar, alcoholic and aqueous media. Ground and excited state pK data and the equilibrium of ground state conformers by excitation spectra and quantum chemical calculations were investigated. The calculations predict a small energy barrier for rotation in the first excited singlet state for the proton transferred tautomers.

Chattopadhyay et al.[106] studied two series of compounds, the first one contains the two compounds above (HPO and HPT), while the second one contains 2-(2`-hydroxyphenyl)benzoxazole (HBO) and 2-(2`-hydroxy phenyl)benzothiazole (HBT) which are susceptible to ground state rotamerisation as well as excited state intermolecular proton transfer (ESIPT) reactions. Semi-empirical AM1-SC1 calculations have been performed to rationalize the photophysical behaviour of the compounds. These calculations suggest that for the first series of compounds, the rotational isomer is present in the ground state of HBO, while HBT has a single conformer under similar circumstances. For the molecules of the other series, existence of rotamers depends very much on the polarity of

the environment. The potential energy curves (PEC) for the ESIPT process in different electronic states of the molecules were investigated theoretically.

2.4.2. *CHARGE TRANSFER*

The UV, NMR and IR spectra of eight di- and trinitrobenzenes containing -Me, -OH, -COOH or nosubstituents, were investigated as their charge-transfer (CT) complexes (CTC) with 2-aminothiazole. The CTC between 2-aminothiazole and nonacidic acceptors involves π- π* transfers are stabilized by proton transfers. The ionization potential of 2-amino-thiazole, the electron affinities of the acceptors and the Coulombic factors of the CTC were established by the CT in the UV of the CTC[(107)]. The direct current electrical conductivity of the charge transfer complexes of some thiazoles and benzothiazoles with certain di- and trinitrobenzene derivatives were investigated[(108)].

2.4.3. *HYDROGEN BOND*

Molecular adducts of 2-aminothiazole derivatives with the carboxylic-acid-substituted heterocyclics; indole-2-carboxylic acid, N-methylpyrrole-2-carboxylicacid and thiophene-2-carboxylic acid were characterized using X-ray powder diffraction and in five cases by single-crystal X-ray diffraction methods. All complexes involve proton transfer,

as indicated by IR spectroscopy, while the five crystal structures display similar H-bonding patterns with the dominant interaction being an R22(8) graph set dimer association between carboxylate groups and amine/heterocyclic N sites[(109)].

The molecules in ethyl 2-amino-4-tert-butyl-1,3-thiazole-5-carboxylate associate via a hydrogen-bonded R22(8) dimer consisting array additionally involving N-H…O interactions to one of the carboxylate O atoms. The 2-aminothiazole molecules in 6-methylimidazo[2,1-b]thiazole-2-amino-1,3-thiazole also associate via an N-H…N hydrogen-bonded R22(8) dimer, with an additional N-H…N interaction to the Nsp^2 atom of the imidazothiazole moiety, creating hydrogen-bonded quartets[(110)]. IR spectra of the free molecules of 2-aminothiazole and their H-bonded complexes of 1:1 composition with acetonitrile, dioxane, tetrahydrofourane, dimethylformamide, dimethylsulfoxide, and hexamethylphosphoramide in CCl_4 were studied in the range of stretching and deformational vibrations of the amino group. The complexes of 1:2 compositions were studied in undiluted aprotic solvents . The absorption band spectral characteristics of monomers and complexes were determined. It was shown that spectral characteristics have practically linear dependence on temperature, and the temperature sensitivity of

spectral characteristics for 1:1 complexes of 2-aminothiazoles with proton acceptors is approximately 10 times higher than for monomers[(111)].

2.4.4. *DIPOLE MOMENTS*

Dipole moment and IR data indicated that substituted benzo-thiazoline (R=H, NH_2, NO_2; X=CH, N) and substituted thiazolinethiones (R=H, NO_2, Br) exist as the thione tautomers in organic solvents. In dioxane the dipole moments decreased as the temperature was increased, while in C_6H_6 they increased with increasing temperature[(112)].

2.4.5. *THERMAL ANALYSIS*

The thermal decomposition of 2-aminothiazole complexes (cobalt, nickel, and copper) in air and argon were investigated by TG and DTG as well as by DTA in nitrogen. The end products from the decomposition in air have been characterized by X-ray powder diffraction[(113)]. Thermal decomposition of a series of substituted 2-nitrosiminobenzothiazolines and of the seleno analog in methanol and of 3-methyl-2-nitrosobenzothiazoline in acetonitrile was investigated experimentally and theoretically. The thermal decomposition followed first-order kinetics[(114)].

2.4.6. *COMPLEXES*

Milton et al.[(115)] prepared the ligands 2-(diphenyl-phosphino)aminothiazole (dppat), 2-(diphenylphosphino)amino-4-methyl-

thiazole (Medppat) and 2-(diphenylphosphino)amino-4-tert-butylthiazole (Budppat). Reactions of these ligands with MCl_2 (COD) gives [MCl(dppat-P,N) (dppat-P)][Cl], [MCl(Medppat-P,N)(Medppat-P)][Cl], and $PtCl_2$ (^{t}Bu-dppat-P_2], respectively. The increased bulk at the 4-position limits the formation of a P, N system in Budppat. The X-ray structure of [PtCl(Medppat-P,N)(Medppat-P)][Cl] reverse that the monodentate ligands has undergone a tautomerism upon coordination.

Copper (I) salts of various anions including thiolates, diethyl dithiocarbamate, diethyl dithiophosphate, and 2-aminothiazole were conveniently synthesized by reducing copper (II) sulfate in aqueous ammonia. The addition of phosphine ligands to several of the products was demonstrated(116). The reaction of $[Os_3(CO)_{10}(CH_3CN)_2]$ with aminothiazole compounds, in CH_2Cl_2 at room temperature, leads to the formation of the new hydride carbonyl clusters. Results from a single-crystal X-ray diffraction analysis shows that the amine group of the ligand is bridging two metal centers of triangular cluster and revealed a double bond between the nitrogen atom of the amine group and the carbon atom of heterocyclic ring(117). The reaction of $[Cu(dien)NO_3]NO_3$ with thiazole, thiazolin and imidazole derivatives gave a new series of mixed-ligand compounds of the general formula $[Cu(dien)(B)NO_3)]NO_3$. The complexes have been characterized by elemental analysis, molar

conductivity and magnetic measurements, as well as by electronic and IR spectral studies. According to these measurements, the possible structure of the compounds is the square pyramidal in the solid state and the square planner in aqueous solution(118).

Spinu et al.(119) prepared N-[2-thienylmethylidene]-2-aminothiazole complexes of Fe(II), Co(II), Ni(II), Cu(II), Zn(II) and Cd(II) and characterized them by elemental analysis, magnetic and spectroscopic measurements. IR and NMR spectra show that N of the azomethine group and S of the thiophene ring take part in coordination.

Magnetic, Mossbauer, ESR, and electronic spectral studies show a distorted octahedral structure for the Fe(II) complex, a square-planar geometry for Ni(II) and Cu(II) complexes and a tetrahedral geometry for Co(II), Zn(II) and Cd(II) complexes. Some new asymmetric 1,1`-disubstituted ferrocene-derived Schiff-bases (HL) were prepared from the 1:1:1 condensation of 1,1`-diacetylferrocene with 2-aminophenol and 2-aminopyrazine/2-aminopyridine/2-aminothiazole and used as ligands in the preparation of their Co(II), Cu(II), Ni(II) and Zn(II) metal chelates. These synthesized ligands and their metal chelates were characterized by their physical, analysis and spectra data. The metal chelates were used for screening against pathogenic bacterial species(120).

THEORETICAL BACKGROUND

3. THEORETICAL BACKGROUND

3.1. AB-INITIO METHODS

The term ″ab-initio″ implies that within the frame of a particular variation or perturbation method no approximations are adopted, though the method itself is a mere approximation to the solution of Schrödinger equation. That means that, unlike in semiempirical methods, no integrals are neglected or approximated by simplified expressions and functions containing empirical parameters, or even replaced by empirical parameters. Explicit inclusion is also made for inner shell electrons. All integrals should be calculated with a high accuracy. ″Ab-initio″ also implies that a nonrelativistic Hamiltonian within the Born Oppenheimer approximation is used.

3.1.1. THE SCHRÖDINGER EQUATION

According to quantum mechanics, the energy and many properties of a stationary state of a molecule can be obtained by solution of the Schrödinger partial differential equation[121].

$$\hat{H}\,\Psi = E\,\Psi \qquad (3\text{-}1)$$

$\hat{H}$ is the Hamiltonian, a differential operator representing the total energy. E is the numerical value of the energy of the state, and Ψ is the wave

function. It depends on both cartesian and spin coordinates of all particles. The Hamiltonian Ĥ, is the sum of kinetic and potential parts,

$$\hat{H} = \hat{T} + \hat{V} \qquad (3\text{-}2)$$

Where: $$\hat{T} = -\frac{h^2}{8\pi^2}\sum_i \frac{1}{m_i}\left(\frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2}\right) \qquad (3\text{-}3)$$

The sum is overall particles i (nuclei and electrons), m_i is the mass of particle i, h is Plank`s constant.

The potential energy operator is the coulomb interaction:

$$\hat{V} = \sum_{i} \sum_{<\ j} \frac{(e_i\ e_j)}{r_{ij}} \qquad (3\text{-}4)$$

Where the sum is over distinct pairs of particles (i , j) with electric charges e_i , e_j separated by a distance r_{ij}.

Within the Born–Oppenheimer approximation[122] equation (1) may be written as:

$$\hat{H}^{elec}\ \psi^{elec}_{(r,R)} = E^{eff}_{(R)}\ \psi^{elec}_{(r,R)} \qquad (3\text{-}5)$$

The main task is to solve, at least approximately, the electronic Schrödinger equation (5), and hence find the effective nuclear potential function E^{eff}_r.

3.1.2. MOLECULAR ORBITAL THEORY

It is an approach to molecular quantum mechanics, which uses one-electron functions or orbitals to approximate the full wavefunction. A molecular orbital, ψ(x,y,z), is a function of the cartesian and spin coordinates of a single electron.

A full antisymmetric many-electron molecular orbital wavefunction for the closed-shell ground state of a molecule with n (even) electrons, can be written down as:

$$\Psi = (n!)^{-1/2} \begin{vmatrix} \psi_1(1)\alpha(1) & \psi_1(1)\beta(1) & \psi_2(1)\alpha(1)\cdots\cdots & \psi_{\frac{n}{2}}(1)\beta(1) \\ \psi_1(2)\alpha(2) & \psi_1(2)\beta(2) & \psi_2(2)\alpha(2)\cdots\cdots & \psi_{\frac{n}{2}}(2)\beta(2) \\ \vdots & \vdots & \vdots & \vdots \\ \vdots & \vdots & \vdots & \vdots \\ \psi_1(n)\alpha(n) & \psi_1(n)\beta(n) & \psi_2(n)\alpha(n)\cdots\cdots & \psi_{\frac{n}{2}}(n)\beta(n) \end{vmatrix} \tag{3-6}$$

This determinant is referred to as a Slater determinant[(123)].

3.1.3. BASIS SET EXPANSIONS

A further restriction is imposed, requiring that the individual molecular orbitals be expressed as linear combinations of a finite set of N prescribed one-electron functions known as basis functions ϕ_μ. Then an individual orbital ψ_i can be written:

$$\psi_i = \sum_{\mu=1}^{N} c_{\mu i}\phi_\mu \tag{3-7}$$

Where $c_{\mu i}$ are the molecular orbital expansion coefficients, these coefficients provide the orbital description with some flexibility.

In simple qualitative versions of molecular orbital theory, atomic orbitals of constituent atoms are used as basis functions. Such treatments are described as linear combination of atomic orbital (LCAO) theories. There are two types of atomic basis functions. The first one is Slater-type atomic orbitals (STO`s), which have exponential radial parts. They are labeled like hydrogen atomic orbitals 1s, 2s, $2p_x$. The second type of basis consists of Gaussian-type atomic functions. These are powers of x, y, z multiplied by exp ($-\alpha r^2$), $\alpha$ being a constant determining the size. GTO`s functions were introduced into molecular orbital computations by Boys(124). They are less satisfactory than STO`s as representations of atomic orbitals. Nevertheless, they have the important advantage that all integrals in the computations can be evaluated explicitly without recourse to numerical integration.

A third possibility is to use linear combinations of Gaussian functions as basis functions. For example, an s-type basis function.

$$\phi_\mu = \sum_{s} d_{\mu s} g_s \ . \tag{3-8}$$

The coefficients $d_{\mu s}$ are fixed. Basis functions of this type are called contracted Gaussians; the individual g_s being termed primitive Gaussians.

3.1.4. TYPES OF BASIS SETS

Minimal Basis Sets – The STO-nG Basis Sets:

The STO-nG[(125)] is a Slater-type orbitals simulated by n Gaussian functions each STO-3G is a minimal basis set because it has only as many orbitals as are necessary to accommodate the electrons of the neutral atom. The main problem of any minimal basis set is its inability to expand or contract its orbitals to fit the molecular environment. One solution to the problem is to use split-valence or double-zeta basis sets.

3.1.4.1. SPLIT-VALENCE AND DOUBLE-ZETA BASIS SETS

In this basis, the atomic orbitals are split into two parts, an inner, compact orbital, and an outer, more diffuse one. The coefficients of these two types of orbitals can be varied independently during constructions of the molecular orbitals in the SCF procedure. Double-zeta basis set is another type of split basis sets. It splits core orbitals as well as valence orbitals, whereas, split-valence basis sets split only valence orbitals.

6-31G[126] is an example of the split-valence basis sets. It means that the core orbitals consist of six and the inner and outer valence orbitals of three and one Gaussian functions, respectively.

3.1.4.2. POLARIZATION BASIS SETS

This type of basis sets incorporates functions of higher angular quantum number than are needed by the atom in its electronic ground state. It provides for displacement of electronic charge away from the nuclear centers, that is, charge polarization.

a) The 6-31G* and 6-31G Polarization Basis Sets**[127,128]

6-31G* basis set is constructed by the addition of a set of six second-order (d-type) Gaussian primitives to the split-valence 6-31G basis set for the description of each heavy (non-hydrogen) atom. A more complete basis set termed 6-31G**, has been constructed. It is identical to 6-31G* except for the addition of a set of Gaussian p-type functions to each hydrogen and helium atom.

b) The 6-311G Basis Sets** [129]

Although they are more flexible than the simple 6-31G* and 6-31G** polarization basis sets, their size has limited their application to only quite small molecular systems. The 6-311G** comprises an inner shell of six s-type Gaussians and an outer (valence) region, which has been split into three parts, represented by three, one, and one primitive, respectively. The

basis set is supplemented by a set of five d-type Gaussians for hydrogen. The 311G "triple" split increases the overall flexibility of the basis set and improves the description of the outer valence region.

3.1.5. VARIATIONAL METHODS AND HARTREE-FOCK THEORY

Up to this point, it has been described how a determinant wave function may be constructed from molecular orbitals, and how the orbitals may, in turn, be expanded in term of a set of basis functions. It remains to specify a method for fixing the coefficients. This is the Hartree-Fock theory[(130)]. It is based on the variational method in quantum mechanics[(131)].

The variational method may be applied to determine optimum orbitals in single-determinant wave functions. For a particular molecular orbital, Ψ_i, where,

$$\Psi_i = \sum_{\nu} C_{i\nu}\phi_{\nu} \,. \qquad (3\text{-}9)$$

The coefficients $c_{\mu i}$ may be adjusted to minimize the expectation value of the energy E\`. The resulting value of E\` will then be as close to the exact energy E as is possible within the limitations imposed by:

a) The single-determinant wavefunction,

b) The particular basis set employed.

C) Hence the best single determinant wavefunction is found by minimizing E` with respect to the coefficients $c_{\mu i}$. This implies the variational equations

$$\frac{\partial E`}{\partial c_{\mu i}} = 0. \quad (\text{all}\, \mu, i) \tag{3-10}$$

3.1.5.1. CLOSED-SHELL SYSTEMS

The variational condition (10) leads to a set of algebraic equations for $c_{\mu i}$. They were derived independently for the closed-shell wave function (6) by Roothaan[132] and by Hall[133]. The Roothaan-Hall equations are:

$$\sum_{\nu=1}^{N} (F_{\mu\nu} - \varepsilon_i S_{\mu\nu}) c_{\nu i} = 0 \qquad . \quad \mu = 1,2,...,N \tag{3-11}$$

with the normalization conditions

$$\sum_{\mu=1}^{N} \sum_{\nu=1}^{N} c^*_{\mu i} S_{\mu\nu} c_{\nu i=1} \quad . \tag{3-12}$$

Here, ε_i is the one-electron energy of molecular orbital ψ_i, $S_{\mu\nu}$ are the elements of an $N \times N$ matrix termed the overlap matrix,

$$S_{\mu\nu} = \int \phi^*_\mu(1)\, \phi_\nu(1)\, dx_1\, dy_1\, dz_1 \,. \tag{3-13}$$

and $F_{\mu\nu}$ are the elements of another $N \times N$ matrix termed the Fock matrix,

$$F_{\mu\nu} = H^{core}_{\mu\nu} + \sum_{\lambda=1}^{N} \sum_{\sigma=1}^{N} P_{\lambda\sigma} \left[(\mu\nu|\lambda\sigma) - \frac{1}{2}(\mu\lambda|\nu\sigma) \right] \tag{3-14}$$

$H^{core}_{\mu\nu}$ is a matrix representing the energy of a single electron in a field of "bare" nuclei. Its elements are

$$H_{\mu\nu}^{core} = \int \phi_\mu^*(1) \hat{H}^{core}(1) \phi_\nu(1)\, dx_1\, dy_1\, dz_1 . \qquad (3\text{-}15a)$$

$$\hat{H}^{core}(1) = -\frac{1}{2}\left(\frac{\partial^2}{\partial x_i^2} + \frac{\partial^2}{\partial y_i^2} + \frac{\partial^2}{\partial z_i^2}\right) - \sum_{A=1}^{M} \frac{Z_A}{r_{1A}} . \qquad (3\text{-}15b)$$

Here Z_A is the atomic number of atom A, and summation is carried out over all atoms. The quantities $(\mu\nu|\lambda\sigma)$ are two-electron repulsion integrals:

$$(\mu\nu|\lambda\sigma) = \iint \phi_\mu^*(1)\phi_\nu(1)\left(\frac{1}{r_{12}}\right)\phi_\lambda^*(2)\phi_\sigma(2)dx_1dy_1dz_1dx_2dy_2dz_2 . \qquad (3\text{-}16)$$

They are multiplied by the elements of the one-electron density matrix. $P_{\lambda\sigma}$.

$$P_{\lambda\sigma} = 2\sum_{i=1}^{occ} c_\lambda c_{\sigma i}^* . \qquad (3\text{-}17)$$

The summation is over occupied molecular orbitals only. The electronic energy is given by:

$$E^{ele} = \frac{1}{2}\sum_{\mu=1}^{N}\sum_{\nu=1}^{N} P_{\mu\nu}(F_{\mu\nu} + H_{\mu\nu}^{core}) \qquad (3\text{-}18)$$

Which when added to the internuclear repulsion, E^{nr},

$$E^{nr} = \sum_{A}^{M}\sum_{<\;B} \frac{Z_A Z_B}{R_{AB}} \qquad (3\text{-}19)$$

an expression for the total energy is obtained.

The Roothaan-Hall equations are not linear since the Fock matrix $F_{\mu\nu}$ itself depends on the molecular orbital coefficient, $c_{\mu i}$, through the density matrix, $P_{\lambda\sigma}$.

3.1.5.2. OPEN –SHELL SYSTEMS

For open-shell systems, the Roothaan-Hall equations need modifications. Simple molecular orbital theory can be extended to open – shell systems in two possible ways. The first is described as spin-restricted Hartree-Fock (RHF) theory(134). In this approach, a single set of molecular orbitals is used, some being doubly occupied and some being singly occupied with an electron of α spin. The coefficients $c_{\mu i}$ are still defined by the expansion (9) and their optimum values are still obtained from the variational conditions, (10).

The second type of molecular orbital theory in common use for open-shell systems is spin-unrestricted Hartree-Fock (UHF) theory(135). In this approach, different spatial orbitals are assigned to α and β electrons. Thus, there are two distinct sets of molecular orbitals ψ_i^{α} and ψ_i^{β} (i= 1,…,N). Since the RHF function is a special case of the UHF function, it follows from the variational principle that the optimized UHF energy must be below the optimized RHF value. UHF functions have the disadvantage that they are not true eigenfunctions of the total spin operator. Thus, UHF wave functions, which designed for doublet states, are contaminated by functions corresponding to states of higher spin multiplicity, such as quartets.

In UHF theory, the two sets of molecular orbitals are defined by two sets of coefficients,

$$\psi_i^{\alpha} = \sum_{\mu=1}^{N} c_{\mu i}^{\alpha}\phi_{\mu}; \qquad \psi_i^{\beta} = \sum_{\mu=1}^{N} c_{\mu i}^{\beta}\phi_{\mu}. \tag{3-20}$$

These coefficients are varied independently, leading to the UHF generalizations of the Roothaan-Hall equations[136]. These are

$$\sum_{\nu=1}^{N}(F_{\mu\nu}^{\alpha} - \varepsilon_i^{\alpha} S_{\mu\nu})c_{\mu i}^{\alpha} = 0 \tag{3-21}$$

$$\sum_{\nu=1}^{N}(F_{\mu\nu}^{\beta} - \varepsilon_i^{\beta} S_{\mu\nu})c_{\mu i}^{\beta} = 0 \qquad \mu = 1,2,..., N. \tag{3-22}$$

Hence, the two Fock matrices are defined by:

$$F_{\mu\nu}^{\alpha} = H_{\mu\nu}^{core} + \sum_{\lambda=1}^{N}\sum_{\sigma=1}^{N}\left[(P_{\lambda\sigma}^{\alpha} + P_{\lambda\sigma}^{\beta})(\mu\nu|\lambda\sigma) - P_{\lambda\sigma}^{\alpha}(\mu\lambda|\nu\sigma)\right]. \tag{3-23}$$

$$F_{\mu\nu}^{\beta} = H_{\mu\nu}^{core} + \sum_{\lambda=1}^{N}\sum_{\sigma=1}^{N}\left[(P_{\lambda\sigma}^{\alpha} + P_{\lambda\sigma}^{\beta})(\mu\nu|\lambda\sigma) - P_{\lambda\sigma}^{\beta}(\mu\lambda|\nu\sigma)\right]. \tag{3-24}$$

The density matrix is also separated into two parts.

$$P_{\mu\nu}^{\alpha} = \sum_{i=1}^{\alpha occ} c_{\mu i}^{\alpha *} c_{\nu i}^{\alpha}; \qquad P_{\mu\nu}^{\beta} = \sum_{i=1}^{\beta occ} c_{\mu i}^{\beta *} c_{\nu i}^{\beta}. \tag{3-25}$$

The integrals $S_{\mu\nu}, H_{\mu\nu}^{core}$ and $(\mu\nu|\lambda\alpha)$ are the same as those already defined in the Roothaan-Hall procedure for closed shell calculations.

3.1.6. MULLIKEN POPULATION ANALYSIS

The electron density functions, $\rho(r)$, is a three-dimensional function defined such that $\rho(r)dr$ is the probability of finding an electron in a small volume element, dr, at some point in space, r- Normalization requires that

$$\int \rho(r)dr = n \tag{3-26}$$

where n is the total number of electrons.

For a single-determinant wavefunction, $\rho(r)$ is given by

$$\rho(r) = \sum_{\mu}^{N}\sum_{\nu}^{N} P_{\mu\nu}\phi_{\mu}\phi_{\nu} \tag{3-27}$$

where $P_{\mu\nu}$ are elements of the density matrix (17).

Allocating the electrons in some fractional manner among the various parts of a molecule (atoms, bonds, etc.) is useful to define the total electronic charge on a particular atom in a molecule. This may imply a quantitative meaning to concepts as electron withdrawing or donating ability. This is done by what is called Mülliken Population Analysis. Integration of Eq. (27) leads to

$$\int \rho(r)dr = \sum_{\mu}^{N}\sum_{\nu}^{N} P_{\mu\nu}S_{\mu\nu} = n \tag{3-28}$$

where $S_{\mu\nu}$ is the overlap matrix. The total electron count is thus composed of individual terms $P_{\mu\nu}S_{\mu\nu}$. Given that ϕ_{μ} are normalized i.e., $S_{\mu\mu} = 1$, the diagonal terms in (28) are just $P_{\mu\mu}$ (the number of electrons directly associated with ϕ_{μ}). This is termed the net population of ϕ_{μ}. The off diagonal components occur in pairs, $P_{\mu\nu}S_{\mu\nu}$ and $P_{\nu\mu}S_{\nu\mu}$, of equal magnitude. Their sum,

$$Q_{\mu\nu} = 2P_{\mu\nu}S_{\mu\nu} \qquad (\mu \neq \nu), \tag{3-29}$$

is referred to as an overlap population. The total electronic charge is now partitioned into two parts; the first associated with individual basis functions, the second with pairs of basis functions:

$$\sum_{\mu}^{N} P_{\mu\mu} + \sum_{\mu}^{N} \sum_{<\ \nu}^{N} Q_{\mu\nu} = n. \qquad (3\text{-}30)$$

It is sometimes desirable to partition the total charge among only the individual basis functions. One way this may be accomplished is to divide the overlap populations $Q_{\mu\nu}$, equally between the basis functions ϕ_{μ} and ϕ_{ν}, adding half to each of the net population $P_{\mu\mu}$ and $P_{\nu\nu}$. This gives a gross population for ϕ_{μ}, defined as

$$q_{\mu} = P_{\mu\mu} + \sum_{\nu \neq \mu} P_{\mu\nu} S_{\mu\nu}\ . \qquad (3\text{-}31)$$

The sum of gross populations for all N basis functions, ϕ_{μ}, is equal to the total electron count,

$$\sum_{\mu}^{N} q_{\mu} = n\ . \qquad (3\text{-}32)$$

This is an arbitrary division of the overlap populations, $Q_{\mu\nu}$, into equal contributions from ϕ_{μ} and ϕ_{ν}.

The gross basis function populations may be used to define gross atomic populations:

$$q_{A} = \sum_{\mu}^{A} q_{\mu}\ . \qquad (3\text{-}33)$$

The summation is carried out for all functions ϕ_μ on a particular atom, A. Finally, a total atomic charge on A may be defined as, where Z_A is the atomic number A. A total overlap population, q_{AB}, between two atoms A and B may be defined in a similar manner,

$$q_{AB} = \sum_{\mu}^{A}\sum_{\nu}^{B} Q_{\mu\nu} \,. \tag{3-34}$$

Here summation is carried out for all μ on atom A and all ν on atom B. Total overlap populations provide quantitative information about the binding between atoms.

3.1.7. MULTI-DETERMINANT WAVEFUNCTIONS

Up to this point, the theory has been developed in terms of single-determinant wavefunctions. It must be recognized that exact wavefunction cannot generally be expressed as single determinants. The primary deficiency of Hartree-Fock theory is the inadequate treatment of the correlation between motions of electrons. In particular, single-determinant wavefunctions take no account of correlation between electrons with opposite spin. This leads to calculated (Hartree-Fock) energies that are above the exact values.

$$\text{E (exact)} = \text{E (Hartree-Fock)} + \text{E (correlation)}. \tag{3-35}$$

The neglect of correlation between electrons of opposite spin leads to a number of qualitative deficiencies in the description of electronic structure and energetics.

There are two methods, will be briefly outlined, that address this problem. Both involve use of a linear combination of Slater determinants, each of which represents an individual electron configuration interaction.

3.1.7.1. FULL CONFIGURATION INTERACTION

Consider a system comprising n electrons described by a set of N functions, ϕ_μ. The ground state HF single-determinant wave function is Ψ_0,

$$\Psi_0 = (n!)^{-1/2} \left|\chi_1 \chi \cdots \chi_n\right| . \qquad (3\text{-}36)$$

Determinant wave functions, other than the HF function Ψ_0, may be constructed replacing one or more of the occupied spin orbitals $\chi_i, \chi_j, \ldots\ldots$ in (36) by virtual spin orbitals $\chi_a, \chi_b, \ldots\ldots.$ The resulting determinants will be denoted as Ψ_s with s > 0. They may be further classified into single-substitution functions, ψ_i^a in which χ_i is replaced by χ_b, double-substitution functions, ψ_{ij}^{ab} in which χ_i replaced by χ_a and χ_j by χ_b, triple-functions and so forth. The general substitution determinant, $\Psi_{ijk\ldots\ldots}^{abc\ldots\ldots}$, with the restrictions i < j < k < .. .. and a < b < c < ….. to avoid repetition of the same configuration.

In the full configuration interaction method, a trial wavefunction,

$$\Psi = a_0 \Psi_0 + \sum_{s>0} a_s \Psi_s \ . \tag{3-37}$$

is used, where the summation is overall substituted determinants. The unknown coefficients, a_s, are then determined by the linear variational method, leading to

$$\sum_s (H_{st} - E_i \delta_{st}) a_{si} = 0 \qquad t = 0,1,2,......... \tag{3-38}$$

Here, H_{st} is a configurational matrix element,

$$H_{st} = \int ....\int \Psi_s H \Psi_t d\tau_1 d\tau_2 ....d\tau_n \ . \tag{3-39}$$

And E_i is energy. Because the determinantal wavefunctions Ψ_s are mutually orthogonal, the overlap matrix S is replaced by a simple delta function, δ_{st}.

The full configuration interaction method represents the most complete treatment possible within the limitations imposed by the basis set. As the basis set becomes more complete, the result of a full configuration interaction treatment will approach the exact solution of the nonrelativistic Schrödinger equation. The full CI method is well defined, size –consistent and variational. However, it is not practical except for very small systems.

3.1.7.2. MÖLLER-PLESSET PERTURBATION THEORY

The perturbation theory of Möller and Plesset[(137)], closely related to many-body perturbation theory, is an alternative approach to the correlation problem. Its aim is still to find the lowest eigenvalue and

corresponding eigenvector of the full Hamiltonian matrix. The approach is not to truncate the matrix as in limited CI, but rather to treat it as the sum of two parts, the second being a perturbation on the first. Möller-Plesset models are formulated by first introducing a generalized electronic Hamiltonian, $\hat{H}_\lambda$, according to

$$\hat{H}_\lambda = \hat{H}_0 + \lambda \hat{V}. \tag{3-40}$$

$\hat{H}_0$ is an operator such that the matrix with elements

$$\int \ldots \int \psi_s \hat{H}_0 \psi_t \, d\tau_1 \, d\tau_2 \ldots d\tau_n \tag{3-41}$$

is diagonal. The perturbation, $\lambda \hat{V}$, is defined by

$$\lambda \hat{V} = \lambda (\hat{H} - \hat{H}_0), \tag{3-42}$$

where $\hat{H}$ is the correct Hamiltonian and λ is dimensionless parameter. $\hat{H}_\lambda$ coincides with $\hat{H}_0$ if $\lambda = 0$, and with $\hat{H}$ of $\lambda = 1$. In MP theory, the zero-order Hamiltonian, $\hat{H}_0$, is taken to be the sum of the one-electron Fock operators. The eigenvalue E_s, corresponding to a particular determinant, ψ_s, is the sum of the one-electron energies, ε_i, for the spin orbitals which are occupied in ψ_s. ψ_λ and E_λ, the exact or full CI (within a given basis set) ground-state wavefunction and energy for a system described by the Hamiltonian $\hat{H}_\lambda$, may now be expanded in powers of λ according to Rayleigh-Schrödinger perturbation theory[138].

$$\psi_Y = \psi^{(0)} + \lambda \psi^{(1)} + \lambda^2 \psi^{(2)} + \ldots \tag{3-43}$$

$$E_{\lambda} = E^{(0)} + \lambda\, E^{(1)} + \lambda^2\, E^{(2)} + \ldots \qquad (3\text{-}44)$$

Practical correlation methods may now be formulated by setting λ =1 and by truncation of the series in Eq. (44) to various orders. It refers to the methods by the highest order energy term allowed, that is, truncation after second-order as MP2, after third order as MP3 and so forth.

The leading terms in expansions (44) are

$$\psi^{(0)} = \psi_0 \qquad (3\text{-}45)$$

$$E^{(0)} = \sum_{i}^{occ} \varepsilon i \qquad (3\text{-}46)$$

$$E^{(0)} + E^{(1)} = \int \ldots \int \psi_0\, \hat{H}\, \psi_0\, d_{T_1}\, d_{T_2} \ldots d_{T_n} \qquad (3\text{-}47)$$

Where ψ_0 is the HF wavefunction and ε_i are the one-electron energies. The MP energy to first-order is thus the HF energy. Higher terms in the expansion involve other matrix elements of the operator $\hat{V}$.

The first order contribution to the wavefunction is

$$\psi^{1)} = \sum_{s>0} (E_0 - E_s)^{-1}\, V_{so}\, \psi_s \qquad (3\text{-}48)$$

where V_{so} are matrix elements involving the perturbation operator, $\hat{V}$,

$$\int \ldots \int \psi_s\, \hat{V}\, \psi_0\, d\tau_1\, d\tau_2 \ldots d\tau_n \qquad (3\text{-}49)$$

It follows that the first-order contribution to the coefficients as in equation (38) is given by

$$a_s^{(1)} = (E_0 - E_s)^{-1}\, V_{so}\,. \qquad (3\text{-}50)$$

The second –order contribution to the Möller-Plesset energy is:

$$E^{(2)} = -\sum_{s}^{D} (E_0 - E_s)^{-1} \left| V_{so} \right|^2 \qquad (3\text{-}51)$$

where $\sum^{D}$ indicates that the summation to be carried out overall double substitutions. This represents the simplest approximate expression for the correlation energy. If ψ_s is the double substitution $i\,j \rightarrow a\,b$, the expression for V_{so} is

$$V_{so} = (i\,j|\,|a\,b) \qquad (3\text{-}52)$$

where $(i\,j|\,|a\,b)$ is a two electron integral over spin orbitals, defined by

$$(i\,j|\,|a\,b) = \iint \chi\ \ i^*(1)\, \chi\, i^*(2)\, (\frac{1}{r_{12}})\, [\chi_a(1)\,\chi_b(2) - \chi_b(1)\,\chi_a(2)]\, d\tau_1\, d\tau_2 \qquad (3\text{-}53)$$

Here, integration is overall coordinates for both electrons. The final formula for the second-order contribution to the energy becomes

$$E^{(2)} = \sum_{i}^{OCC} \sum_{<\,j} \sum_{a} \sum_{<\,b}^{virt} (\varepsilon_a + \varepsilon_b - \varepsilon_i - \varepsilon_j)^{-1} \left| (ij|\,|ab) \right|^2 \qquad (3\text{-}54)$$

Unlike the simple CID and CISD configuration interaction schemes, MP2 requires only a partial transformation of the two-electron integrals of equation (16) into a spin orbital basis.

The third-order contribution to the Möller-Plesset energy also follows directly from Rayleigh-Schrödinger theory. It is

$$E^{(3)} = \sum_{s}^{D} \sum_{t}^{D} (E_0 - E_s)^{-1}\, (E_0 - E_t)^{-1}\, V_{os}\, (V_{st} - V_{oo}\delta_{st})\, V_{to} \qquad (3\text{-}55)$$

where the summations are again carried out over double substitutions only. The matrix elements V_{st} between different double substitutions require a full integral transformation or other techniques of comparable complexity[(139)]. At the fourth-order of theory, single, triple, and quadruple substitutions also contribute, since they have nonzero Hamiltonian matrix elements with the double substitutions. The triple substitutions are the most difficult computationally, and some computations have been carried out using only singles, doubles, and quadruples. This partial fourth-order level of theory is termed MP4SDQ.

MP2, MP3, and MP4 energy expressions are well defined. They can be applied quite widely. They do satisfy the size-consistency requirement, as do Möller-Plesset energy expansions terminated at any order. This follows since full CI is size consistent with the Hamiltonian $\hat{H}_\lambda$ for any value of λ; hence, individual terms in equation (44) must be size-consistent. In this respect, the perturbation expressions are more satisfactory than the CID or CISD methods for determining correlation energies. On the other hand, perturbation theory results, terminated at any order, are no longer variational since they are not derived as expectation values of the Hamiltonian.

3.1.7.3. DENSITY FUNCTIONAL THEORY (DFT)

The practical implementation of DFT leads to effective one-electron Schrödinger equations or ″Kohn-Sham equations″ which are very similar to the Hartree-Fock equations, except that in the Kohn-Sham equations, the orbital-dependent exchange operator of the Hartree-Fock equations are formally replaced by an exchange-correlation operator that depends only on the total electron density (and spin density in spin-polarized calculations). This makes the form of the matrix elements simpler and the one-particle wave functions can be represented not only by Gaussian-type orbitals, but also by a variety of other functions such as Slater-type orbitals(140,141), numerical functions(142-144), plane waves(145,146), or augmented plane waves(147-149). Completely numerical (″basis set free″) solutions of the density functional equations have been proposed as well(150). It turns out, however, that Gaussian-type basis functions are appealing in molecular DFT calculations for the same reasons as in Hartree-Fock theory.

THEORETICAL ASPECTS

SCF equations and single point energies

In density functional theory(151-154), the total energy, including electron correlation effects, is written in the form

$$E[\rho] = T[\rho] + U[\rho] + E_{xc}[\rho] \quad . \qquad (3\text{-}56)$$

Here, T is a kinetic energy term, U is the electrostatic interaction energy between all electrons and nuclei, and E_{xc} is the exchange-correlation energy of the system.

The total electron density ρ in Eq. (56) can be related to single-particle wave functions by

$$\rho(\mathrm{r}) = \sum_{occ} |\psi_i(\mathrm{r})|^2 , \qquad (3\text{-}57)$$

where the summation extends over all occupied electronic levels.

A variational principle applied to Eq. (56), together with the definition of the one-particle wave functions (57), leads to effective one-particle Schrödinger equations, usually referred to as Kohn-Sham equations, of the form

$$\mathbf{H}\psi_i = \varepsilon_i \psi_i , \qquad (3\text{-}58)$$

where **H** represents a one-particle Hamiltonian operator, ψ_i are one-electron wave functions [molecular orbitals (MOs)], and ε_i can be interpreted as one-electron energies (MO energies).

As a consequence of the form for the total energy expression in Eq. (56), the effective one-particle Hamiltonian operator **H** can be written as

$$\mathbf{H} \equiv [-1/2\nabla^2 + V_c(\mathrm{r}) + \mu_{xc}(\mathrm{r})]. \qquad (3\text{-}59)$$

Hartree atomic units are used here with $h^2/(4\pi^2 m) = 1$ and $e^2 = 1$. V_c is the electrostatic (or Coulomb) potential

$$V_c = V_N + V_e \qquad (3\text{-}60)$$

consisting of the electron-nuclear attraction

$$V_N(\mathrm{r}) = -\sum_{\alpha} Z_\alpha / |\mathbf{R}_\alpha - \mathrm{r}| \qquad (3\text{-}61)$$

And the electron- electron repulsion

$$V_e(\mathrm{r}) = \int \rho(\mathrm{r}')\, 1/|\mathrm{r}-\mathrm{r}'|d\mathrm{r}'. \qquad (3\text{-}62)$$

Here, $\mathbf{R}_\alpha$ denotes the position of atom α with the atomic number Z_α. The sum in Eq. (61) extends over all atoms of the molecular system.

The exchange-correlation potential is expressed by the term μ_{xc} , which is related to the exchange-correlation energy by

$$\mu_{xc} = \partial E_{xc} / \partial \rho \qquad (3\text{-}63)$$

In the so-called local density approximation (LDA)[152], the total exchange-correlation energy is approximated by

$$E_{xc} \approx \int \rho(\mathrm{r})\varepsilon_{xc}[\rho(\mathrm{r})]d\mathrm{r}, \qquad (3\text{-}64)$$

where $\varepsilon_{xc}[\rho(\mathrm{r})]d\mathrm{r}$ is the exchange-correlation energy in a volume element $d\mathrm{r}$ in which the local density is $\rho(\mathrm{r}); \varepsilon_{xc}[\rho]$ is the exchange-correlation energy per electron in a correlated (i.e., interacting) electron system of constant density ρ. In the present implementation, we use the form for as $\varepsilon_{xc}[\rho]$ given by Vosko, Wilk, and Nusair[155].

The molecular orbitals ψ_i are represented by Gaussians in the same way as in the Hartree-Fock method

$$\psi_i = \sum_p c_{ip} g_p \qquad (3\text{-}65)$$

with $\{g_p; p = 1,...,N\}$ being a set of contracted Gaussian basis functions.

Following Sambe and Felton[156], the electron density is also expanded in a set of Gaussian-type functions. Because of the finite number of Gaussians in this auxiliary set, this representation amounts to the approximation

$$\rho(\mathrm{r}) \approx \rho(\mathrm{r}') = \sum_r \rho_r g_r \tag{3-66}$$

with $\{g_r; r = 1,...,N_r\}$ being a set of auxiliary basis functions.

Similarly, the exchange-correlation potential $\mu_{xc}(r)$ is expanded in another auxiliary set of Gaussian-type functions $\{g_s; s = 1,...,N_s\}$ in the form

$$\mu_{xc}(\mathrm{r}) = \sum_s \mu_s g_s. \tag{3-67}$$

Substituting expressions (59)-(67) in Eq. (58) and applying a variational principle analogous to that used in Hartree-Fock theory leads to a system of equations that determines the coefficients in expansion (10):

$$(H_{pq} - \varepsilon_i S_{pq})c_{iq} = 0. \tag{3-68}$$

These equations have to be solved in a self-consistent procedure. The matrix elements in Eq (68) are given as follows:

$$H_{pq} = h_{pq} + \sum_r \rho_r [pq\|r] + \sum_s \mu_s [pqs] \tag{3-69}$$

and

$$S_{pq} = [pq]. \tag{3-70}$$

Equations (68) and (69) contain one-electron and two-electron integrals defined by

$$h_{pq} \equiv \int g_p(\mathrm{r})\left(-1/2\nabla^2 - \sum_\alpha Z_\alpha / |\mathbf{R}_\alpha - \mathrm{r}|\right) g_q(\mathrm{r}) d\mathrm{r}, \tag{3-71}$$

$$[pq\|r] \equiv \int\int g_p(\mathrm{r}) g_q(\mathrm{r})(1/|\mathrm{r}-\mathrm{r}'|) g_r(\mathrm{r}') d\mathrm{r} d\mathrm{r}', \tag{3-72}$$

$$[pqs] \equiv \int g_p(\mathrm{r}) g_q(\mathrm{r}) g_s(\mathrm{r}) d\mathrm{r}, \tag{3-73}$$

$$[pq] \equiv \int g_p(\mathrm{r}) g_q(\mathrm{r}) d\mathrm{r}. \tag{3-74}$$

It should be noted that the one-electron integrals h_{pq}, as well as the overlap integrals S_{pq}, are identical to those found in the Roothaan-Hartree-Fock equations[(157)]. Without the density expansion of Eq. (66), the term $\sum_r \rho_r (pq\|r)$ of Eq. (69) would contain

$$\sum_i c_{ir} c_{is} \int\int g_p(\mathrm{r}) g_q(\mathrm{r})(1/|\mathrm{r}-\mathrm{r}'|) g_r(\mathrm{r}') g_s(\mathrm{r}') d\mathrm{r} d\mathrm{r}', \tag{3-75}$$

which represent the familiar four-index, two-electron Coulomb integrals of the Hartree-Fock theory. The last term in Eq. (69) can be compared formally with the exchange integrals of the Hartree-Fock theory. However, as discussed above, the term includes correlation effects.

Following Dunlap[(158)], the density fitting coefficients ρ_r, in Eq. (66) are defined such that the Coulomb energy

$$\Delta \equiv \int\int \delta\rho(\mathrm{r})(1/|\mathrm{r}-\mathrm{r}'|)\delta\rho(\mathrm{r}') d\mathrm{r} d\mathrm{r}' \tag{3-76}$$

arising from the difference between the fitted and original density

$$\delta\rho(\mathrm{r}) \equiv \rho(\mathrm{r}) - \rho'(\mathrm{r}) \tag{3-77}$$

is minimized while maintaining charge conservation. Using the definition of the density matrix **P**,

$$P_{pq} = \sum_i c_{ip} c_{iq} \tag{3-78}$$

with the summation extending over all occupied molecular orbitals, we find the coefficients ρ_r to be determined by

$$\rho_r = \sum_{r'} C_{rr'}^{-1} \left\{ \sum_{pq} P_{pq} [pq \| r'] - \Lambda \int g_r(\mathrm{r}) d\mathrm{r} \right\} \tag{3-79}$$

The Lagrange multipliers Λ guarantee charge conservation[158]. The matrix C is defined by its elements

$$C_{rr'} = [r \| r'] \equiv \iint g_r(\mathrm{r})(1/|\mathrm{r}-\mathrm{r}'|) g_{r'}(\mathrm{r}') d\mathrm{r} d\mathrm{r}'. \tag{3-80}$$

All the integrals necessary to calculate the density fitting coefficients ρ_r can be obtained from analytic, Coulomb-type integrals.

The fitting coefficients for the exchange-correlation potential in Eq. (66) are given by the following relations:

$$\mu_s = \sum_{s'} S_{ss'}^{-1} \int g_{s'}(\mathrm{r}) \mu_{xc}(\mathrm{r}) d\mathrm{r} \tag{3-81}$$

with $S_{ss'}$ being overlap matrix elements defined in Eq. (67). The evaluation of the integrals in Eq. (81) is done numerically as will be discussed below. Recently, a method for the variational fitting of the exchange-correlation potential has been formulated[159], but not yet implemented in the present approach.

Based on the self-consistent charge density, Dunlap[158] derived an expression for the LDA total energy which is exact to second order in the error of the density fit of Eq. (66). The explicit form, which resembles the corresponding expression of the Hartree-Fock theory, is

$$E_{LDA} = \sum_{pq} P_{pq} \left(h_{pq} + \sum_r \rho_r [pq \| r] + \sum_s \varepsilon_s [pqs] \right) - \frac{1}{2} \sum_{rr'} \rho_r \rho_{r'} [r \| r'] + U_N. \qquad (4\text{-}82)$$

Similar to the expansion of the exchange-correlation potential given in Eq. (67), the exchange-correlation energy needed for the total energy expression (82) is expanded in a set of Gaussian-type functions in the form

$$\varepsilon_{xc}(\mathrm{r}) = \sum_s \varepsilon_s g_s. \qquad (4\text{-}83)$$

In fact, the same set of functions $\{g_s\}$ is used as in the expansion of μ_{xc}. The integrals $[r \| r']$ are defined in Eq. (80)

$$U_N = 1/2 \sum_{\alpha\alpha'} Z_\alpha Z_{\alpha'} / |R_\alpha - R_{\alpha'}| \qquad (4\text{-}84)$$

denotes the Coulomb repulsion energy between all nuclei.

THEORETICAL METHOD

All calculations were performed using the PC GAMESS [6.4][160,161] program. The equilibrium structure of each tautomer under investigation has been fully optimized within the C_1 symmetry constraint by the gradient procedure, at the ab initio (RHF)[134], Möller-Plesset (MP2)[137] and Density Functional Theory (DFT) levels. The Density Functional Theory (DFT) method was used with the hybrid of Becke`s non-local three parameter exchange and correlated functional with the empirical correlation functional of Lee-Yang-Parr (LYP): B3LYP[162,163]. Many basis sets were tested and used starting from 6-31+G*[127] and enlarging them up to 6-311++G**[129]. The choice of these basis sets was based on obtaining the reliable properties of hydrogen-bonded systems, because they posses sufficient diffuseness and regular flexibility. The vibrational frequencies were calculated for each stationary point to characterize its nature. The transition states are those with an imaginary frequency.

The tautomeric equilibrium between tautomers A and B is described as:

$$A \underset{}{\overset{K_T}{\rightleftharpoons}} B \tag{3.85}$$

The equilibrium constants for each species were calculated by using the following equation:

$$K_T = e^{-(\delta\Delta G_f / RT)} \tag{3.86}$$

Where K_T is the tautomeric equilibrium constant between the tautomers.

$$K_T = \frac{[B]}{[A]} \qquad (3.87)$$

R is the gas constant (1.987×10^{-3} Kcal/mol).

T is the temperature (298.15 K).

$\delta\Delta G_f$ is the difference between the Gibbs free energy of the given tautomer with respect to the most stable one.

$$\delta\Delta G_f = \Delta G_{(B)} - \Delta G_{(A)} \qquad (3.88)$$

$\Delta G_{(B)}$ and $\Delta G_{(A)}$ are the Gibbs free energies of each tautomer (A and B). The Gibbs free energy of each tautomer (i) at a given temperature T can be expressed as

$$\Delta G_{f(i)} = \Delta H_{f(i)} - T\Delta S_{f(i)} \qquad (3.89)$$

Where (i) = A, B

ΔH_f is the difference in enthalpy of formation between the two tautomers.

ΔS_f is the difference in entropy change between the two tautomers.

Thus, $\delta\Delta G_f$ and pK_T can be calculated if both of ΔH_f and ΔS_f are known.

ΔH_f is calculated using the equation

$$\Delta H_f = \Delta E + \Delta(ZPE) + \Delta(TC) \qquad (3.90)$$

Where ΔE is the reaction energy and equals

$$\Delta E = E_{t(B)} - E_{t(A)} \qquad (3.91)$$

Where $E_{t(i)}$ is the calculated total energy, of a tautomer.

$$\Delta ZPE = ZPE_{(B)} - ZPE_{(A)} \quad \text{Zero point energy correction} \qquad (3.92)$$

$$\Delta TC = TC_{(B)} - TC_{(A)} \qquad \text{Thermal energy correction} \tag{3.93}$$

The pK_T values of the studied molecules were calculated by means of the following equations:

$$pK_T = \frac{\delta\Delta G}{2.303RT} \tag{3.94}$$

To estimate the effect of the medium on the structure and relative stabilities of the tautomers of the studied compounds, Solute-Solvent interactions were taken into account using the most recent version of PCM method. This method, which is implemented in the GAMESS6.4 program, includes cavity effects directly in quantum mechanical calculations[(164-166)]. Solvent effects were investigated in water (polar solvent) [ε=76] and carbon tetrachloride [ε=36.44] as apolar solvent using the B3LYP/6-311++G** level. Single point calculations were performed using the gas phase geometry obtained at the same level assuming that no change in structure took place in solutions. The solvation energy was taken as the difference between the energies in solution and gas phase. The relative free energies in solution ΔG°_{soln}, were calculated using the relation:

$$\Delta G^{\circ}_{soln} = \Delta G^{\circ}_{g} + \Delta G^{\circ}_{s} \tag{3.95}$$

where ΔG°_{g} is the free energy change in gas phase and ΔG°_{s} is the solvation free energy.

All calculations were performed using PC program, Intel Pentium 4, M processor 2.7 GH_Z, 256 MB DD RAM, 80 GB hard schijf.

RESULTS AND DISCUSSION

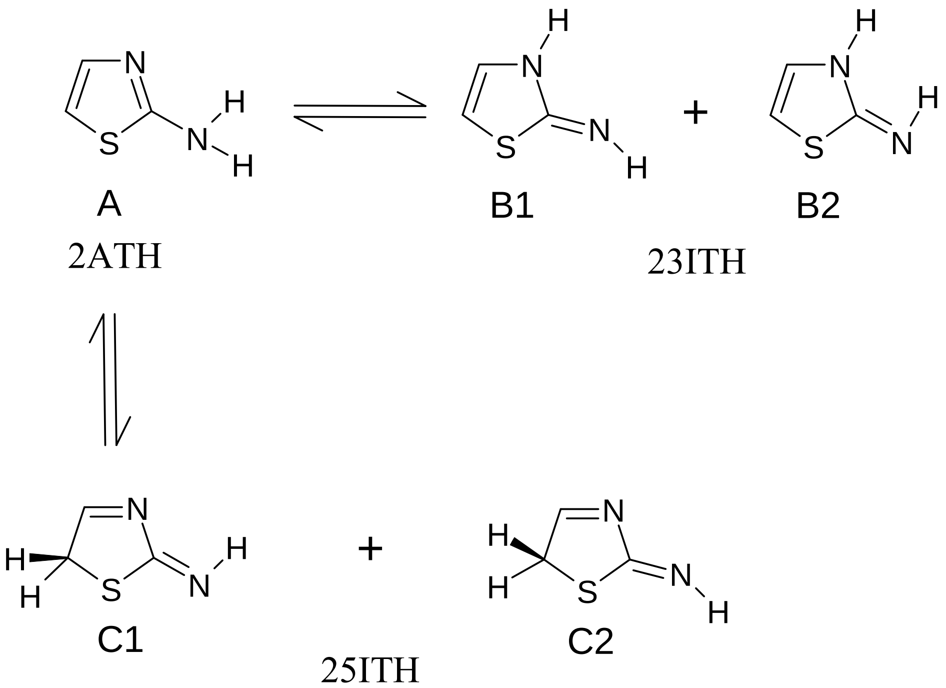
4. RESULTS AND DISCUSSION

4.1. AMINO-THIAZOLES

4.1.1. GEOMETRY:

4.1.1.1. 2-AMINOTHIAZOLE

A great deal of interest is shown in the tautomeric structure of amino-aza heterocycles. In case of 2-aminothiazole, IR[31-33], X-ray[34,35] UV[36,37] and H^{1}NMR[38-41] spectral data and pK$_a$ measurements[67,167] indicate that the amino form is usually present in larger amounts than the imino form. This also is apparent from the reactivity data of some of its derivatives[168,169]. The equilibrium for tautomers of such molecule can be given as:

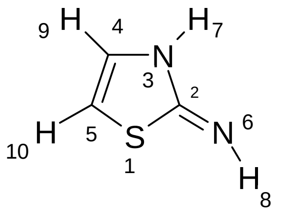


GAS PHASE

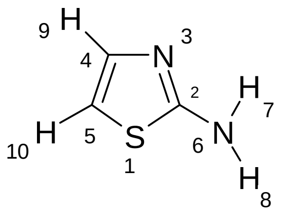
The structure and numbering system of the studied aminothiazoles are presented in Fig. (1). The geometry of the three tautomers of 2-aminothiazole **2ATH**, thiazole-2(3H)-imino **23ITH**, thiazole-2(5H)-imino **25ITH**, was obtained at RHF/6-31+G* and the results are depicted in Table (1). Two experimental results, X-ray[34] and vibrational[33] data, are given in the same table for comparison. The calculations show that 2-aminothiazole **2ATH** is a planer compound but the exocyclic N-atom is slightly out of the thiazole ring plane. The values of the bond lengths of the thiazole ring are not of pure single or double bonds, which indicate the aromaticity character of this azole system. This is also proved by the corresponding bond order values, Table (1). The RHF/6-31+G* level overestimates the single bonds in the ring; C_2S_1, S_1C_5, N_3C_4 and slightly underestimates the double bonds, with a maximum error equals = 0.025Å. This means that it fails to describe well the aromaticity of this system. Enlarging the basis set by additional polarization, diffuse functions and splitting of valency orbitals does not much affect the accuracy of the RHF level results, Table (1).

On the other hand, including of electron correlations using both B3LYP and MP2 methods, elongate the calculated double bonds by only 0.006Å while the maximum error of a single bond length is 0.015Å in case

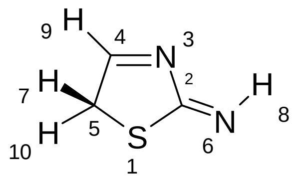
Fig (1): Structure and numbering system of 2-aminothiazole (**2ATH**), 4-aminothiazole (**4ATH**), and 5-aminothiazole (**5ATH**).



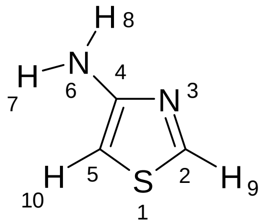
Thiazole-2(3H)-imino
23ITH



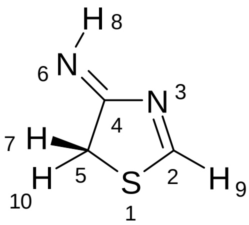
2-Aminothiazole
2ATH



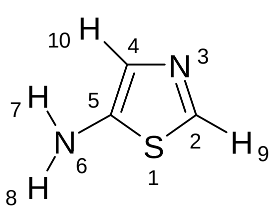
Thiazole-2(5H)-imino
25ITH



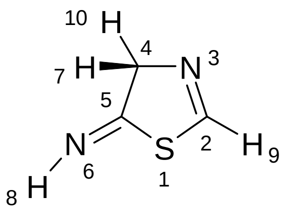
4-Aminothiazole
4ATH



Thiazole-4(5H)-imino
45ITH



5-Aminothiazole
5ATH



Thiazole-5(4H)-imino
54ITH

Table (1): Geometrical parameters of the two isomers (**2ATH** and **23ITH**) calculated at the **RHF** level with different basis sets.

	RHF / 6-31+G*	**RHF / 6-311+G***	**RHF /6-311+G****	**RHF/6-311++G****
Bond length Å				
Bond Order				
S_1C_2 (1.746)* (1.724)[a]	1.745 (1.783)[a] 1.731][b]	1.745 (1.784) [1.730]	1.745 (1.783) [1.730]	1.745 (1.784) [1.730]
	1.041 (0.950) [0.960]	*1.000 (0.869) [1.025]*	*0.995 (0.869) [1.030]*	*0.985 (0.886) [1.046]*
S_1C_5 (1.739)* (1.731)[a]	1.743 (1.766) [1.775]	1.745 (1.767) [1.777]	1.744 (1.766) [1.776]	1.744 (1.766) [1.777]
	0.979 (0.888) [0.899]	*1.070 (0.977)[0.995]*	*1.025 (0.932) [0.947]*	*1.032 (0.948) [0.957]*
C_2N_3 (1.306)* (1.303)[a]	1.278 (1.372) [1.325]	1.275 (1.372) [1.324]	1.275 (1.372) [1.324]	1.275 (1.372) [1.324]
	1.647 (1.150) [1.359]	*1.728 (1.087) [1.228]*	*1.708 (1.075) [1.249]*	*1.803 (1.079) [1.275]*
N_3C_4 (1.392)* (1.372)[a]	1.380 (1.381) [1.369]	1.380 (1.382) [1.368]	1.380 (1.382) [1.368]	1.380 (1.382) [1.368]
	1.070 (0.911) [1.167]	*0.966 (0.863) [1.163]*	*0.969 (0.846) [0.991]*	*0.876 (0.768) [0.940]*
C_4C_5 (1.310)* (1.367)[a]	1.338 (1.324) [1.338]	1.335 (1.322) [1.336]	1.335 (1.322) [1.336]	1.335 (1.322) [1.336]
	1.986 (2.123) [2.025]	*2.039 (2.163) [2.059]*	*1.900 (2.030) [1.934]*	*2.056(2.243) [2.119]*
C_2N_6 (1.330)* (1.387)[a]	1.371 (1.257) [1.302]	1.370 (1.253) [1.300]	1.369 (1.253) [1.301]	1.369 (1.253) [1.301]
	1.111 (1.873) [1.401]	*1.189 (2.013) [1.316]*	*1.101 (1.855) [1.277]*	*1.107 (1.913) [1.269]*
N_6H_7	0.999 (2.550) [1.388]	0.995 (2.552)[1.387]	0.996 (2.555) [1.379]	0.996 (2.555) [1.378]
	0.792 --- [0.333]	*0.838 --- [0.310]*	*0.948 --- [0.399]*	*0.947 --- [0.402]*
N_3H_7	2.491 (0.996) [1.326]	2.492 (0.992) [1.323]	2.495 (0.993) [1.313]	2.495 (0.993) [1.313]
	--- *(0.772) [0.305]*	--- *(0.750) [0.305]*	--- *(0.892) [0.443]*	--- *(0.904) [0.452]*
Bond Angle degree				
$N_3C_2S_1$ (115.8)* (123.6)[a]	115.2 (107.3) [112.8]	115.2 (107.2) [112.8]	115.2 (107.2) [112.9]	115.2 (107.2) [112.9]
$C_4N_3C_2$ (110.2)* (110.1)[a]	110.6 (116.3) [113.6]	110.7 (116.3) [113.6]	110.7 (116.3) [113.6]	110.7 (116.3) [113.6]
$C_5C_4N_3$ (116.2)* (124.8)[a]	116.7 (114.3) [114.4]	116.7 (114.5) [114.5]	116.7 (114.5) [114.5]	116.7 (114.5) [114.5]
$N_6C_2S_1$ (119.8)* (121.3)[a]	121.0 (129.6) [141.1]	120.9 (129.4) [141.1]	120.9 (129.3) [141.1]	120.9 (129.3) [141.1]
$H_7N_6C_2$ (119.0)[a]	113.1 (119.1) [77.0]	113.3 (119.2) [77.0]	113.5 (119.3) [76.6]	113.4 (119.3) [76.6]
Dihedral Angle degree				
$N_3C_2S_1N_6$	177.0 (180.0) [180.0]	177.1 (180.0) [180.0]	177.2 (180.0) [180.0]	177.2 (180.0) [179.9]
$C_4N_3C_2S_1$	0.1 (0.0) [0.0]	0.1 (0.0) [0.0]	0.0 (0.0) [0.0]	0.0 (0.0) [0.0]
$C_5C_4N_3C_2$	0.4 (0.0) [0.0]	0.4 (0.0) [0.0]	0.4 (0.0) [0.0]	0.4 (0.0) [0.0]
$N_6C_2S_1N_3$	177.0 (180.0) [180.0]	177.1 (180.0) [180.0]	177.2 (180.0) [180.0]	177.2 (180.0) [179.9]
$H_7N_6C_2N_3$	15.6 (0.1) [0.0]	15.4 (0.1) [0.0]	15.3 (0.1) [0.0]	15.4 (0.1) [0.0]

Table (1): Continue.

	RHF / 6-31+G*	RHF / 6-311+G*	RHF /6-311+G**	RHF/6-311++G**
Charge				
N_3	-0.358 (-0.580)[a] [-0.555][b]	-0.210 (-0.347) [-0.381]	-0.209 (-0.236)[-0.303]	-0.227 (-0.227) [-0.296]
C_4	-0.149 (-0.048) [-0.093]	-0.271 (-0.237) [-0.391]	-0.173 (-0.118) [-0.206]	-0.215 (-0.120) [-0.223]
C_5	-0.379 (-0.381)[-0.413]	-0.364 (-0.327) [-0.325]	-0.225 (-0.228)[-0.220]	-0.257 (-0.317) [-0.301]
N_6	-0.822 (-0.700) [-0.987]	-0.620 (-0.576) [-0.959]	-0.416 (-0.483)[-0.700]	-0.344 (-0.421) [-0.651]
H_7	0.432 (0.489) [0.570]	0.378 (0.465) [0.609]	0.272 (0.332) [0.432]	0.277 (0.355) [0.445]
Dipole Moment D	1.652 (3.162) [1.070]	1.627 (3.130) [1.054]	1.605 (3.137) [1.092]	1.601 (3.136) [1.090]

( )[a]: correspond to imino, [ ][b]: correspond to TS.
Values in italic refer to **Bond Order**.
***** Results (X-ray) obtained from Ref. (34).
[a] Results (IR) obtained from Ref. (33).

of MP2 level. The calculated bond angles value at all levels show an error of about 1°, Tables (1,3). Therefore, it is expected, for MP2 and B3LYP methods that increasing the basis set size by additional higher momentum angular orbitals will be sufficient for very accurate estimation of the ground state properties of our system. The accuracy of MP2 and B3LYP results is also found for the geometry of various heterocycles[(170-172)].

The Mülliken charge density at different centers of **2ATH** are given in Tables (1-3) and also the value of the dipole moment. This charge distribution proves the existence of an intermolecular association by hydrogen bonding between the substituent amino group of one molecule and the basic thiazolinic nitrogen of another molecule especially in the solid state[(33,34)]. The negative charge on exocyclic nitrogen atom (N_6) is higher than that on endocyclic atom (N_3) in all levels. While the atomic charge on C_5 is less than that on C_4. The computed gas phase dipole moment of **2ATH** is 1.601, 1.762 and 1.705 D at the RHF, MP2 and B3LYP levels with the 6-311++G** bases set. No expect data are available for dipole moment to compare with our results. This means that **2ATH** is a polar molecule, which seems to be dominated by the lone pairs of exo- and endocyclic nitrogen atoms with little perturbing effect of the sulfur lone pair.

Table (2): Geometrical parameters of the two isomers (**2ATH** and **23ITH**) calculated at the **MP2** and **B3LYP** levels with different basis sets.

	MP2		**B3LYP**	
	6-31+G*	6-311++G**	6-31+G*	6-311++G**
Bond Length Å				
Bond Order				
S_1C_2	1.743 (1.784)[a] [1.730][b]	1.739 (1.780) [1.728]	1.768 (1.810) [1.747]	1.767 (1.809) [1.745]
	1.008 (0.890) [0.944]	*0.950 (0.812) [1.004]*	*1.063 (0.945) [1.031]*	*0.996 (0.907) [1.072]*
S_1C_5	1.726 (1.750) [1.751]	1.722 (1.747) [1.747]	1.751 (1.770) [1.781]	1 .749 (1.768) [1.780]
	0.992 (0.885) [0.929]	*1.012 (0.883) [0.952]*	*0.982 (0.929) [0.930]*	*1.027 (0.965) [0.973]*
C_2N_3	1.313 (1.383) [1.348]	1.310 (1.383) [1.347]	1.303 (1.386) [1.348]	1.298 (1.385) [1.345]
	1.453 (1.156) [1.301]	*1.620 (1.072) [1.200]*	*1.569 (1.263) [1.380]*	*1.758 (1.140) [1.303]*
N_3C_4	1.379 (1.382) [1.376]	1.376 (1.381) [1.375]	1.381 (1.386) [1.375]	1.379 (1.385) [1.372]
	1.086 (0.943) [1.116]	*0.892 (0.791) [0.917]*	*1.128 (0.989) [1.194]*	*0.930 (0.863) [1.000]*
C_4C_5	1.369 (1.352) [1.366]	1.370 (1.352) [1.367]	1.361 (1.346) [1.360]	1.356 (1.341) [1.356]
	1.663 (1.814) [1.715]	*1.742 (1.962) [1.816]*	*1.749 (1.879) [1.777]*	*1.908 (2.101) [1.976]*
C_2N_6	1.389(1.288) [1.335]	1.389 (1.285) [1.335]	1.380 (1.278) [1.325]	1.377 (1.272) [1.321]
	1.058 (1.686) [1.419]	*1.063 (1.709) [1.282]*	*1.106 (1.772) [1.439]*	*1.163 (1.893) [1.373]*
N_6H_7	1.017 (2.559) [1.446]	1.013 (2.562) [1.431]	1.014 (2.570) [1.420]	1.011 (2.571) [1.410]
	0.762 --- [0.353]	*0.909 --- [0.392]*	*0.795 --- [0.360]*	*0.934 --- [0.407]*
N_3H_7	2.494 (1.015) [1.323]	2.486 (1.010) [1.295]	2.522 (1.011) [1.334]	2.524 (1.009) [1.326]
	--- (0.694) [0.316]	*--- (0.860) [0.485]*	*--- (0.742) [0.353]*	*--- (0.898) [0.491]*
Bond Angle degree				
$N_3C_2S_1$	115.1 (107.0) [112.1]	115.3 (107.0) [112.3]	114.9 (106.6) [112.2]	114.8 (106.4) [112.2]
$C_4N_3C_2$	110.1 (116.6) [113.7]	109.9 (116.6) [113.5]	110.6 (117.0) [113.9]	110.8 (117.0) [113.9]
$C_5C_4N_3$	116.0 (113.3) [113.0]	116.0 (113.3) [112.9]	116.7 (114.0) [114.0]	116.7 (114.2) [114.1]
$N_6C_2S_1$	121.2 (130.9) [140.3]	121.1 (130.6) [140.1]	121.1 (130.7) [141.3]	121.1 (130.4) [141.3]
$H_7N_6C_2$	110.9 (118.5) [77.4]	110.6 (118.7) [76.6]	113.0 (118.6) [77.0]	113.4 (118.7) [76.6]
Dihedral Angle degree				
$N_3C_2S_1N_6$	174.1 (180.0) [-168.2]	180.0 (180.0) [-166.5]	176.0 (180.0) [-174.1]	176.4 (180.0) [-174.6]
$C_4N_3C_2S_1$	0.7 (0.0) [5.9]	0.7 (0.1) [7.0]	0.2 (0.0) [3.6]	0.1 (0.0) [3.2]
$C_5C_4N_3C_2$	0.3 (0.0) [-5.6]	0.2 (0.0) [-6.6]	0.3 (0.0) [-3.3]	0.4 (0.0) [-3.0]
$N_6C_2S_1N_3$	174.1 (180.0) [-168.2]	180.0 (180.0) [-166.5]	176.0 (180.0) [-174.1]	176.4 (180.0) [-174.6]
$H_7N_6C_2N_3$	14.9 (0.0) [3.0]	16.2 (0.1) [2.9]	16.0 (0.0) [1.8]	15.4 (0.0) [1.7]

Values in italic refer to **Bond Order**.
( )[a]: correspond to imino, [ ][b]: correspond to TS.

Table (2): Continue.

	MP2		B3LYP	
	6-31+G*	6-311++G**	6-31+G*	6-311++G**
Charge				
N_3	-0.259 (-0.469)[a] [-0.321][b]	-0.116 (-0.109) [-0.081]	-0.257 (-0.385) [-0.319]	-0.146 (-0.069) [-0.146]
C_4	-0.195 (-0.088) [-0.135]	-0.283 (-0.187) [-0.307]	-0.213 (-0.115) [-0.157]	-0.295 (-0.204) [-0.316]
C_5	-0.353 (-0.364) [-0.367]	-0.211 (-0.261) [-0.211]	-0.275 (-0.304) [-0.309]	-0.143 (-0.217) [-0.181]
N_6	-0.765 (-0.617) [-0.766]	-0.285 (-0.353) [-0.441]	-0.701 (-0.609) [-0.759]	-0.214 (-0.342) [-0.430]
H_7	0.418 (-0.464) [0.440]	0.266 (0.333) [0.310]	0.399 (0.427) [0.440]	0.257 (0.317) [0.337]
Dipole Moment D	1.756 (2.887) [1.678]	1.762 (2.807) [1.754]	1.728 (2.783) [1.137]	1.705 (2.728) [1.109]

( )[a]: correspond to imino, [ ][b]: correspond to TS.

Table (3): Geometrical parameters of the two isomers (**2ATH** and **25ITH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

	MP2 6-311++G**			**B3LYP** 6-311++G**		
Bond Length Å						
Bond Order						
S_1C_2	1.739	(1.779)[a]	[1.786][b]	1.767	(1.805)	[1.814]
	0.951	*(0.724)*	*[1.015]*	*0.996*	*(0.857)*	*[1.056]*
S_1C_5	1.722	(1.804)	[1.774]	1.749	(1.823)	[1.825]
	1.012	*(0.804)*	*[0.810*	*1.027*	*(0.924)*	*[0.803]*
C_2N_3	1.310	(1.429)	[1.401]	1.298	(1.425)	[1.379]
	1.620	*(1.202)*	*[0.959]*	*1.758*	*(1.125)*	*[1.135]*
N_3C_4	1.376	(1.282)	[1.311]	1.379	(1.271)	[1.313]
	0.892	*(1.324)*	*[1.455]*	*0.930*	*(1.611)*	*[1.482]*
C_4C_5	1.370	(1.504)	[1.457]	1.356	(1.506)	[1.445]
	1.742	*(0.799)*	*[1.055]*	*1.908*	*(0.962)*	*[1.184]*
C_2N_6	1.389	(1.273)	[1.346]	1.377	(1.262)	[1.326]
	1.063	*(1.846)*	*[1.411]*	*1.163*	*(2.053)*	*[1.556]*
N_6H_7	1.012	(4.525)	[1.350]	1.011	(4.540)	[1.383]
	0.879	---	*[0.488]*	*0.934*	---	*[0.486]*
C_5H_7	4.377	(1.094)	[1.670]	4.421	(1.094)	[1.706]
	---	*(0.975)*	*[0.504]*	---	*(0.967)*	*[0.500]*
Bond Angle degree						
$N_3C_2S_1$	115.3	(112.8)	[114.5]	114.8	(111.9)	[114.2]
$C_4N_3C_2$	109.9	(111.3)	[102.4]	110.8	(112.7)	[102.3]
$C_5C_4N_3$	116.0	(120.2)	[115.8]	116.7	(120.3)	[116.1]
$N_6C_2S_1$	121.1	(121.9)	[104.9]	121.1	(121.9)	[107.8]
$H_7N_6C_2$	110.6	(110.0)	[86.6]	113.4	(110.7)	[83.6]
Dihedral Angle degree						
$N_3C_2S_1N_6$	180.0	(180.0)	[126.3]	176.4	(180.0)	[133.5]
$C_4N_3C_2S_1$	0.7	(180.0)	[88.2]	0.1	(180.0)	[91.7]
$C_5C_4N_3C_2$	0.2	(0.0)	[1.3]	0.4	(0.0)	[0.2]
$N_6C_2S_1N_3$	180.0	(180.0)	[126.3]	176.4	(180.0)	[133.5]
$H_7N_6C_2N_3$	16.2	(120.2)	[5.4]	15.4	(120.1)	[4.2]

( )[a]: correspond to imino, [ ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (3): Continue.

Charge	MP2 6-311++G**			B3LYP 6-311++G**		
N_3	-0.116	(-0.007)[a]	[0.033][b]	-0.146	(-0.017)	[-0.013]
C_4	-0.283	(0.072)	[-0.358]	-0.295	(-0.042)	[-0.300]
C_5	-0.211	(-0.683)	[-0.224]	-0.143	(-0.507)	[-0.245]
N_6	-0.285	(-0.217)	[-0.185]	-0.214	(-0.237)	[-0.175]
H_7	0.266	(0.198)	[0.170]	0.257	(0.196)	[0.219]

( )[a]: correspond to imino, [ ][b]: correspond to TS .

The optimized geometrical parameters of the two imino tautomers **23ITH** and **25ITH** [B, C] are given in Tables (2 and 3). Comparing to the geometry of **2ATH** molecule the two imino forms [B, C] are also planer, with geometry totally different from the corresponding amino tautomer, due to disappearance of ring aromaticity. The bonds C_2S_1 and C_2N_3 become more longer i.e. pure single bonds and the C_2N_6 or C_4N_3 bonds shorten by about 0.1 Å reaching to a pure double bond length. These findings are reflected on the corresponding bond order values, cf Tables (2 and 3).

The charge distribution on different centers changes on going from amino to imino forms. A negative charge transfers to both the exocyclic nitrogen atom N_6 and carbon atom C_5 in case of the imino form leading to increase in its dipole moment value, Tables (2 and 3). Therefore, one expects a pronounced solvent effect on the equilibrium ratio of amino and imino forms in different solvents of different polarities. The imino form can exist in two conformers according to the orientation of the exocyclic N-H group, B_1 and B_2 or C_1 and C_2, respectively. The form B_1 is found to be more stable than B_2 by 3.5 Kcal/mol while C_1 is less in energy than C_2 by 1.23 Kcal/mol at B3LYP/6-311++G**. Both B_1 and C_1 conformers will be used as the imino forms during this part of calculations.

4.1.1.2. 4- AND 5-AMINOTHIAZOLES

The literature does not contain a lot about 5-amino isomer with respect to the other two position isomers. This may be due to the difficulty of its preparation. Table (4) shows the optimized geometrical parameters of 4-aminothiazole **4ATH** and its 4-iminothiazole **45ITH** calculated at both B3LYP and MP2 / 6-311++G** levels. Comparing to 2-amino-thiazole **2ATH**, the bonds C_2S_1 and C_5S_1 become much shorter while the C-NH_2 and C_4-C_5 bonds elongate by 0.013Å. These differences are reflected in the various bond order values of the two compounds. The ground state geometrical parameters of **5ATH** isomer are collected in Table (5). Both of C-NH_2 and C_4-C_5 bonds elongate while the C_4-N_3 bond shortens. This is attributed to the difference in extent of nitrogen lone pair in conjugation in the different isomers, Table (6).

The dipole moment of **4ATH** is 1.574 D while it is 1.705 D for the **2ATH** isomer and 2.786 D for **5ATH**, at the B3LYP level. This means that dipole vector of the exocyclic nitrogen atom governs the total dipole of aminothiazole system more than the lone pair of N or S atoms in the ring. The dipole moment of the corresponding imino forms of **2ATH** and **4ATH** are higher than that of their amino forms while for the five isomer **5ATH**, the reverse trend is found. Therefore, their tautomerization processes will be affected by the solvent polarity in different directions.

Table (4): Geometrical parameters of the two isomers (**4ATH** and **45ITH**) calculated at the **MP2** and the **B3LYP / 6-311++G****.

	MP2 6-311++G**			**B3LYP** 6-311++G**		
Bond Length Å *Bond Order*						
S_1C_2	1.713	(1.746)[a]	[1.731][b]	1.735	(1.766)[a]	[1.754][b]
	1.080	*(0.951)*	*[1.085]*	*1.130*	*(1.022)*	*[1.155]*
S_1C_5	1.709	(1.810)	[1.776]	1.736	(1.833)	[1.809]
	0.923	*(0.682)*	*[0.848]*	*0.886*	*(0.758)*	*[0.893]*
C_2N_3	1.317	(1.289)	[1.314]	1.299	(1.277)	[1.302]
	1.371	*(1.530)*	*[1.374]*	*1.534*	*(1.644)*	*[1.484]*
N_3C_4	1.368	(1.420)	[1.375]	1.378	(1.416)	[1.372]
	1.068	*(0.906)*	*[1.068]*	*1.100*	*(1.027)*	*[1.164]*
C_4C_5	1.382	(1.527)	[1.449]	1.372	(1.533)	[1.456]
	1.737	*(0.765)*	*[1.098]*	*1.827*	*(0.883)*	*[1.185]*
C_4N_6	1.398	(1.276)	[1.324]	1.390	(1.266)	[1.314]
	0.968	*(1.862)*	*[1.423]*	*1.081*	*(2.006)*	*[1.534]*
N_6H_7	1.011	(2.767)	[1.350]	1.009	(2.781)	[1.352]
	0.887	---	*[0.422]*	*0.917*	---	*[0.438]*
C_5H_7	2.701	(1.091)	[1.470]	2.710	(1.089)	[1.483]
	---	*(0.966)*	*[0.424]*	---	*(0.978)*	*[0.434]*
Bond Angle degree						
$N_3C_2S_1$	115.4	(120.5)	[119.6]	115.3	(119.8)	[119.0]
$C_4N_3C_2$	110.1	(110.4)	[105.6]	111.0	(112.0)	[107.2]
$C_5C_4N_3$	115.2	(113.9)	[119.5]	115.2	(113.5)	[119.6]
$N_6C_4N_3$	118.1	(125.3)	[131.1]	117.5	(125.6)	[131.8]
$H_7N_6C_4$	113.7	(109.9)	[77.4]	115.8	(110.8)	[78.7]
Dihedral Angle degree						
$N_3C_2H_9C_4$	179.4	(180.0)	[171.7]	179.8	(180.0)	[172.9]
$C_4N_3C_2S_1$	0.1	(0.0)	[-5.2]	0.1	(0.0)	[-4.3]
$C_5C_4N_3C_2$	0.2	(0.1)	[14.5]	0.2	(0.0)	[13.5]
$N_6C_4N_3C_2$	175.9	(179.9)	[-147.4]	177.1	(180.0)	[-150.1]
$H_7N_6C_4N_3$	150.2	(119.8)	[158.9]	154.7	(119.4)	[159.2]

(   )[a]: correspond to imino, [   ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (4): Continue.

Charge	MP2 6-311++G**			B3LYP 6-311++G**		
N_3	-0.099	(-0.049)[a]	[-0.033][b]	-0.118	(-0.054)	[-0.053]
C_4	-0.346	(-0.245)	[-0.143]	-0.481	(-0.281)	[-0.171]
C_5	-0.372	(-0.256)	[-0.302]	-0.305	(-0.271)	[-0.318]
N_6	0.059	(-0.352)	[-0.502]	0.082	(-0.279)	[-0.419]
H_7	0.243	(0.229)	[0.269]	0.235	(0.221)	[0.278]

( )[a]: correspond to imino, [ ][b]: correspond to TS.

Table (5): Geometrical parameters of the two isomers (**5ATH** and **54ITH**) calculated at the **MP2** and **B3LYP** levels with different basis sets.

	MP2 6-311++G**			**B3LYP** 6-311++G**		
Bond Length Å *Bond Order*						
S_1C_2	1.729	(1.770)[a]	[1.795][b]	1.761	(1.792)[a]	[1.841][b]
	1.015	*(0.878)*	*[0.876]*	*1.046*	*(0.948)*	*[0.898]*
S_1C_5	1.726	(1.785)	[1.730]	1.750	(1.814)	[1.744]
	0.950	*(0.802)*	*[1.036]*	*0.977*	*(0.838)*	*[1.108]*
C_2N_3	1.313	(1.087)	[1.292]	1.291	(1.086)	[1.270]
	1.486	*(0.836)*	*[1.589]*	*1.682*	*(0.871)*	*[1.774]*
N_3C_4	1.370	(1.452)	[1.410]	1.376	(1.450)	[1.412]
	1.067	*(0.907)*	*[0.986]*	*1.118*	*(0.992)*	*[1.064]*
C_4C_5	1.380	(1.523)	[1.441]	1.369	(1.529)	[1.448]
	1.665	*(0.838)*	*[1.002]*	*1.820*	*(0.913)*	*[1.075]*
C_5N_6	1.402	(1.274)	[1.327]	1.393	(1.260)	[1.313]
	1.057	*(1.949)*	*[1.411]*	*1.164*	*(2.152)*	*[1.528]*
N_6H_7	1.013	(2.726)	[1.376]	1.011	(2.778)	[1.373]
	0.913	---	*[0.380]*	*0.945*	---	*[0.398]*
C_4H_7	2.644	(1.093)	[1.477]	2.670	(1.094)	[1.502]
	---	*(0.935)*	*[0.463]*	---	*(0.944)*	*[0.480]*
Bond Angle degree						
$N_3C_2S_1$	115.5	(119.8)	[118.4]	114.7	(119.1)	[117.0]
$C_4N_3C_2$	110.0	(111.2)	[109.7]	111.5	(112.8)	[112.0]
$C_5C_4N_3$	116.1	(111.5)	[112.2]	116.0	(111.7)	[111.8]
$N_6C_5C_4$	129.0	(122.3)	[108.4]	129.3	(123.3)	[108.4]
$H_7N_6C_5$	111.4	(110.1)	[70.3]	113.4	(109.7)	[70.2]
Dihedral Angle degree						
$N_3C_2S_1H_9$	178.2	(179.8)	[179.0]	179.3	(180.0)	[-178.5]
$C_4N_3C_2S_1$	1.0	(179.3)	[1.3]	1.0	(180.0)	[1.2]
$C_5C_4N_3C_2$	0.3	(5.2)	[9.7]	0.3	(0.1)	[9.0]
$N_6C_5C_4N_3$	173.4	(173.0)	[150.7]	174.9	(179.9)	[153.2]
$H_7N_6C_5C_4$	4.9	(127.0)	[5.9]	9.3	(121.3)	[7.0]

( )[a]: correspond to imino, [ ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (5): Continue.

Charge	MP2 6-311++G**			B3LYP 6-311++G**		
N_3	-0.071	(-0.024)[a]	[-0.017][b]	-0.073	(-0.031)	[-0.013]
C_4	-0.266	(-0.624)	[-0.625]	-0.262	(-0.600)	[-0.620]
C_5	-0.208	(-0.038)	[-0.060]	-0.206	(-0.024)	[-0.004]
N_6	-0.339	(-0.213)	[-0.258]	-0.265	(-0.227)	[-0.279]
H_7	0.253	(0.231)	[0.261]	0.241	(0.228)	[0.267]

( )[a]: correspond to imino, [ ][b]: correspond to TS.

Table (6): Comparing geometrical parameters of 2-, 4-, and 5-aminothiazole calculated at the **B3LYP** and **MP2** / **6-311++G****.

Bond Length Å	S_1C_2	S_1C_5	C_2N_3	N_3C_4	C_4C_5	CN_6	N_6H	C_5H_7
Exp.*	1.746	1.750	1.306	1.392	1.310	1.300	---	---
Exp.[a]	1.724	1.731	1.304	1.372	1.367	1.387	0.900	0.920
2ATH	1.767	1.749	1.298	1.379	1.356	1.377	1.011	4.421
	1.739	*1.722*	*1.310*	*1.376*	*1.370*	*1.389*	*1.013*	*4.377*
4ATH	1.735	1.736	1.299	1.378	1.372	1.390	1.009	2.710
	1.713	*1.709*	*1.317*	*1.368*	*1.382*	*1.398*	*1.011*	*2.701*
5ATH	1.761	1.750	1.291	1.376	1.369	1.393	1.011	2.670
	1.729	*1.726*	*1.313*	*1.370*	*1.380*	*1.402*	*1.013*	*2.644*
23ITH	1.809	1.768	1.385	1.385	1.341	1.272	2.571	---
	1.780	*1.747*	*1.383*	*1.381*	*1.352*	*1.285*	*2.562*	
25ITH	1.805	1.823	1.425	1.271	1.506	1.262	4.540	1.094
	1.779	*1.804*	*1.429*	*1.282*	*1.504*	*1.273*	*4.525*	*1.094*
45ITH	1.766	1.833	1.277	1.416	1.533	1.266	2.781	1.089
	1.746	*1.810*	*1.289*	*1.420*	*1.527*	*1.276*	*2.767*	*1.091*
54ITH	1.792	1.814	1.086	1.450	1.529	1.260	2.778	1.094
	1.770	*1.785*	*1.087*	*1.452*	*1.523*	*1.274*	*2.726*	*1.093*
TS_1	1.745	1.780	1.345	1.372	1.356	1.321	1.410	---
	1.728	*1.747*	*1.347*	*1.375*	*1.367*	*1.335*	*1.431*	
TS_2	1.814	1.825	1.379	1.313	1.445	1.326	1.383	1.706
	1.786	*1.774*	*1.401*	*1.311*	*1.457*	*1.346*	*1.350*	*1.670*
TS_3	1.754	1.809	1.302	1.372	1.456	1.314	1.352	1.483
	1.731	*1.776*	*1.314*	*1.375*	*1.449*	*1.324*	*1.350*	*1.470*
TS_4	1.841	1.744	1.270	1.412	1.448	1.313	1.373	1.502
	1.795	*1.730*	*1.292*	*1.410*	*1.441*	*1.327*	*1.021*	*1.477*

Values in italic refer to **MP2**.
* Results (X-ray) obtained from Ref. (34).
[a] Results (IR) obtained from Ref. (33).

Table (6): Continue.

	Bond Angle degree				
	$N_3C_2S_1$	$C_4N_3C_2$	$C_5C_4N_3$	N_6	H_7
Exp.*	115.8	110.2	116.2	119.8	---
Exp.[a]	123.6	110.1	$C_5C_4H_9$ 124.8	121.3	119.0
2ATH	114.8 *115.3*	110.8 *109.9*	116.7 *116.0*	$N_6C_2S_1$ 121.1 *121.1*	$H_7N_6C_2$ 113.4 *110.6*
4ATH	115.3 *115.4*	111.0 *110.1*	115.2 *115.2*	$N_6C_4N_3$ 117.5 *118.1*	$H_7N_6C_4$ 115.8 *113.7*
5ATH	114.7 *115.5*	111.5 *110.0*	116.0 *116.1*	$N_6C_5C_4$ 129.3 *129.0*	$H_7N_6C_5$ 113.4 *111.4*
23ITH	106.4 *107.0*	117.0 *116.6*	114.2 *113.3*	$N_6C_2S_1$ 130.4 *130.6*	$H_7N_3C_2$ 118.7 *118.7*
25ITH	111.9 *112.8*	112.7 *111.3*	120.3 *120.2*	$N_6C_2S_1$ 121.9 *121.9*	$H_7C_5C_4$ 110.7 *110.0*
45ITH	119.8 *120.5*	112.0 *110.4*	113.5 *113.9*	$N_6C_4N_3$ 125.6 *125.3*	$H_7C_5C_4$ 110.8 *109.9*
54ITH	119.1 *119.8*	112.8 *111.2*	111.7 *111.5*	$N_6C_5C_4$ 123.3 *122.3*	$H_7C_4N_3$ 109.7 *110.1*
TS_1	112.2 *112.3*	113.9 *113.5*	114.1 *112.9*	$N_6C_2S_1$ 141.3 *140.1*	$H_7N_3C_2$ 76.6 *76.6*
TS_2	114.2 *114.5*	102.3 *102.4*	116.1 *115.8*	$N_6C_2S_1$ 107.8 *104.9*	$H_7N_6C_2$ 83.6 *86.6*
TS_3	119.0 *119.6*	107.2 *105.6*	119.6 *119.5*	$N_6C_4N_3$ 131.8 *131.1*	$H_7N_6C_4$ 78.7 *77.4*
TS_4	117.0 *118.4*	112.0 *109.7*	111.8 *112.2*	$N_6C_5C_4$ 108.4 *108.4*	$H_7C_4C_5$ 70.2 *70.3*

Values in italic refer to **MP2**.

4.1.2. ***IONIZATION POTENTIAL***

It is interesting to compare between the three position isomers **2ATH**, **4ATH** and **5ATH** and their imino isomers with respect to their calculated IP and energy gap ΔE_g values. MP2 results compare well with the available experimental values[(173)], while those calculated at B3LYP level are underestimated, Tables (7 and 8). The position of $-NH_2$ group does not appreciably affect the E_{HOMO} and E_{LUMO} of aminothiazoles, **2ATH** and **5ATH** have nearly the same IP (8.536 and 8.528 eV) and IP of **4ATH** is 8.370 eV. On the other hand, E_{LUMO} of **2ATH** and **4ATH** is 1.113 and 1.105 eV while that for **5ATH** is 0.982 eV. The least stabilized HOMO is found for **23ITH** -8.085 eV while the other three imino forms have nearly same IP. The order of IP of all aminothiazoles tautomers is (MP2 results)

23ITH < 4ATH < 5ATH ≈ 2ATH < 45ITH ≈ 25ITH < 54ITH.

The order of the energy gap (ΔE_g) which is considered as a measure of the reactivity of the compound is as follows (MP2 results) **23ITH** (8.986 eV) **< 4ATH** (9.475 eV) **< 5ATH** (9.510 eV) **< 2ATH** (9.649 eV) **< 25ITH** (10.474 eV) **< 45ITH** (10.694 eV) **< 54ITH** (10.857 eV) which means that **2ATH** is less reactive than both of **4ATH** and **5ATH** isomers while the least reactive one is the imino **54ITH**.

Table (7): Total energy in gas, water (w), and CCl_4, net charges, thermal correction **TC,** Ionization Potential **IP**, ΔE_g, Dipole moment in gas, water, and CCl_4 of 2-, 4-, and 5-aminothiazole calculated at the **B3LYP/6-311++G**.**

Parameter	2ATH	4ATH	5ATH	23ITH	25ITH	45ITH	54ITH	TS_1	TS_2	TS_3	TS_4
E_t(gas) a.u.	-624.50691	-624.50360	-624.49506	-624.49454	-624.48823	-624.49177	-624.48542	-624.42032	-624.33761	-624.38934	-624.37651
ZPE	45.02	44.92	44.91	44.76	44.70	44.93	44.72	41.06	41.07	41.01	40.53
TC	48.42	48.31	48.32	48.15	47.98	48.21	48.06	44.41	44.01	44.08	43.68
S	74.30	74.31	74.50	74.49	74.24	74.82	75.17	74.38	71.46	72.49	72.94
E_{HOMO} eV	-6.074	-5.910	-6.085	-5.704	-6.868	-7.018	-7.100				
E_{LUMO} eV	-0.629	-0.950	-0.816	-0.411	-1.986	-1.913	-1.181				
ΔE_g eV	5.445	4.960	5.269	5.293	4.882	5.105	5.919				
IP eV	6.074	5.910	6.085	5.704	6.868	7.018	7.100				
***IP** eV	8.52										
E_t(W) a.u.	-624.51708	-624.51167	-624.50641	-624.50592	-624.50060	-624.50170	-624.49505	-624.42593	-624.34606	-624.39614	-624.38447
E_t(CCL_4) a.u.	-624.51124	-624.50751	-624.49979	-624.49940	-624.49338	-624.49606	-624.48951	-624.42265	-624.34115	-624.39227	-624.37981
Dipole Moment D											
D.M(gas)	1.705	1.574	2.786	2.728	4.359	2.147	1.438	1.109	1.989	0.841	2.297
D.M(W)	2.293	2.033	3.714	3.678	6.123	3.019	1.953	1.461	2.793	1.055	3.140
D.M(CCL_4)	1.928	1.771	3.162	3.143	5.071	2.495	1.620	1.248	2.306	0.911	2.615
Charge:											
N_3	-0.146	-0.118	-0.073	-0.069	-0.017	-0.054	-0.031	-0.146	-0.013	-0.053	-0.013
C_4	-0.295	-0.481	-0.262	-0.204	-0.042	-0.281	-0.600	-0.316	-0.300	-0.171	-0.620
C_5	-0.143	0.082	-0.206	-0.217	-0.507	-0.279	-0.024	-0.181	-0.245	-0.419	-0.004
N_6	-0.214	-0.305	-0.265	-0.342	-0.237	-0.271	-0.227	-0.430	-0.175	-0.318	-0.279
H_7	0.257	0.235	0.241	0.317	0.196	0.221	0.228	0.337	0.219	0.278	0.267

***IP** Results (U.V. and visible spectra) obtained from Ref. (173).
Zero point energy **ZPE**, Thermal correction **TC** Kcal/mol, and entropy **S** cal/mol-K.

Table (8): Total energy in gas, water (w), and CCl_4, net charges, thermal correction **TC**, Ionization Potential **IP**, ΔE_g, Dipole moment in gas, water, and CCl4 of 2-, 4-, and 5-aminothiazole at the **MP2/6-311++G**.**

Parameter	2ATH	4ATH	5ATH	23ITH	25ITH	45ITH	54ITH	TS_1	TS_2	TS_3	TS_4
E_t(gas) a.u.	-623.45805	-623.45600	-623.44763	-623.43856	-623.43514	-623.43846	-623.43186	-623.37011	-623.29375	-623.33729	-623.32581
ZPE	45.37	45.11	45.26	44.43	45.14	45.21	44.89	41.73	41.42	41.57	41.06
TC	48.77	48.58	48.68	47.58	48.45	48.57	47.75	44.90	44.34	44.59	44.15
S	74.44	75.03	74.64	72.81	74.83	77.14	71.38	73.11	71.26	72.20	72.57
E_{HOMO} eV	-8.536	-8.370	-8.528	-8.085	-9.663	-9.652	-9.777				
E_{LUMO} eV	1.113	1.105	0.982	0.901	0.811	1.042	1.080				
ΔE_g eV	9.649	9.475	9.510	8.986	10.474	10.694	10.857				
IP eV	8.536	8.370	8.528	8.085	9.663	9.652	9.777				
*IP eV	8.52										
Dipole moment D											
D.M(gas)	1.762	1.854	2.635	2.807	4.237	2.107	1.657	1.754	2.295	0.788	2.534
Charge:											
N_3	-0.116	-0.099	-0.071	-0.109	-0.007	-0.049	-0.024	-0.081	0.033	-0.033	-0.017
C_4	-0.283	-0.346	-0.266	-0.187	0.072	-0.245	-0.624	-0.307	-0.358	-0.143	-0.625
C_5	-0.211	0.059	-0.208	-0.261	-0.683	-0.352	-0.038	-0.211	-0.224	-0.502	-0.060
N_6	-0.285	-0.372	-0.339	-0.353	-0.217	-0.256	-0.213	-0.441	-0.185	-0.302	-0.258
H_7	0.266	0.243	0.253	0.333	0.198	0.229	0.231	0.310	0.170	0.269	0.261

***IP** Results (U.V. and visible spectra) obtained from Ref. (173).
Zero point energy **ZPE**, thermal correction **TC** Kcal/mol, and entropy **S** cal/mol-K.

4.1.3. ***<u>ENERGIES AND RELATVE STABILITIES</u>***

4.1.3.1. 2-AMINOTHIAZOLE

The gas phase calculated total energies and the relative stabilities of the different tautomers of **2ATH** are given in Tables (7-9). **2ATH** form is found to be the most stable one at all levels of calculations while the least one is **25ITH,** i.e. the order of stability is

2ATH > 23ITH > 25ITH

The difference in energy between these three species decreases with inclusion of polarized functions and splitting in basis set. The two imino tautomers **25ITH** and **23ITH** have 11.72 and 7.76 Kcal/mol higher than the amino form at the B3LYP/6-311++G** level, the corresponding values at MP2 level are 14.38 and 12.23 Kcal/mol. The addition of both (ZPE) and (TC) does not affect the order of relative stabilities. These results are in good agreement with the available experimental data[31,41,69] where the amino form is the only detected one.

The tautomerization process **2ATH** $\rightleftharpoons$ **23ITH** passes through a barrier of 68.64, 54.34 and 55.18 Kcal/mol at the three levels and 6-311++G** bases set. The ZPE correction of these values gives the following results 60.79, 46.64 and 48.26 Kcal/mol respectively, while the Gibbs free energy change ΔG of the process is calculated at the three levels

Table (9): Relative stabilities conversion barrier **ΔE***(kcal/mol), activation energy **E_a**(kcal/mol), reaction enthalpy **ΔH** (kcal/mol), and the Gibbs free energy change **ΔG** (Kcal/mol), and equilibrium constant **K** of 2-, 4-, and 5-aminothiazole calculated at the **B3LYP**, **MP2**, and **RHF** levels / **6-311++G****.

	2ATH=23ITH	**2ATH=25ITH**	**4ATH=45ITH**	**5ATH=54ITH**
ΔE*	54.34 (55.18) [68.64]	106.24 (103.10)	71.69 (74.49)	74.39 (76.44)
Ea	46.64 (48.26) [60.79]	98.47 (95.31)	64.14 (67.55)	65.96 (68.30)
ΔE	7.76 (12.23) [8.62]	11.72 (14.38)	7.42 (11.01)	6.05 (9.90)
ΔH	7.23 (10.10) [8.29]	10.96 (13.83)	7.33 (11.10)	5.60 (8.60)
ΔG	7.18 (10.59) [8.06]	10.98 (13.71)	7.17 (10.47)	5.40 (9.57)
LogK	-5.2593 (-7.7590) [-5.9070]	-8.0475 (-10.05)	-5.2589 (-7.6720)	-3.9574 (-7.0126)
K	1.82×10^{5} (5.74×10^{7}) [8.07×10^{5}] 2.1×10^{4} * 2.0×10^{4} [a]	1.12×10^{8} (1.12×10^{10})	1.82×10^{5} (4.70×10^{7})	9.07×10^{3} (1.03×10^{7})

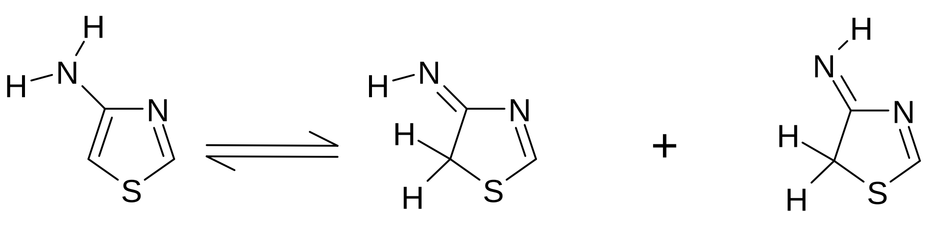
Values in parenthesis refer to **MP2**, and values in two brackets refer to **RHF**.
* Results obtained from Ref. (67).
[a] Results obtained from Ref. (167).

and give the values 8.06, 7.18 and 10.59 Kcal/mol. These values are very similar to the corresponding relative stability values of enthalpy term ΔH.

The entropy contribution is only (0.2 cal/mol) indicating that its effect on the Gibbs free energy is very small and thus the $T\Delta S$ term value can be neglected for such tautomerism. Therefore, the enthalpic term is dominated in the determination of the equilibrium constant K= [amino] / [imino] which has the values: 8.07×10^5, 1.82×10^5 and 5.74×10^7 at the RHF, B3LYP, and MP2 levels. The tautomeric constant (K) for **2ATH** $\rightleftharpoons$ **23ITH** is measured experimentally[67,167] in water. The value is 2.1×10^4 or 2.0×10^4 i.e. our calculated value overestimates the experimental one specially that by MP2 level.

4.1.3.2. 4- AND 5-AMINOTHIAZOLES

The effect of position of amino group on the energetic and thermo-dynamic properties of the studied tautomeric process is studied. The tautomeric process (1,3-hydrogen transfer) of 4-aminothiazole **4ATH** investigated as shown:



The total energy of the forms **4ATH** (A, C) (gas phase) are given in Tables (7 and 8). 4-Iminothiazole **45ITH** (4B) is less stable than (C) tautomer by 3.68 Kcal/mol at the B3LYP/6-311++G** level, therefore (C) will be considered as the imino form for the proceeding calculations. The total energy of the isomer 4-aminothiazole **4ATH** is higher than that of the corresponding 2-isomer **2ATH** by 2.08 and 1.29 Kcal/mol at the B3LYP and MP2 levels of calculations. The least stable aminothiazole is **5ATH** one. It is higher in energy than **2ATH** by 7.44 and 6.54 Kcal/mol at the two levels, Fig (2). This is can be explained in terms of their resonance contributions.

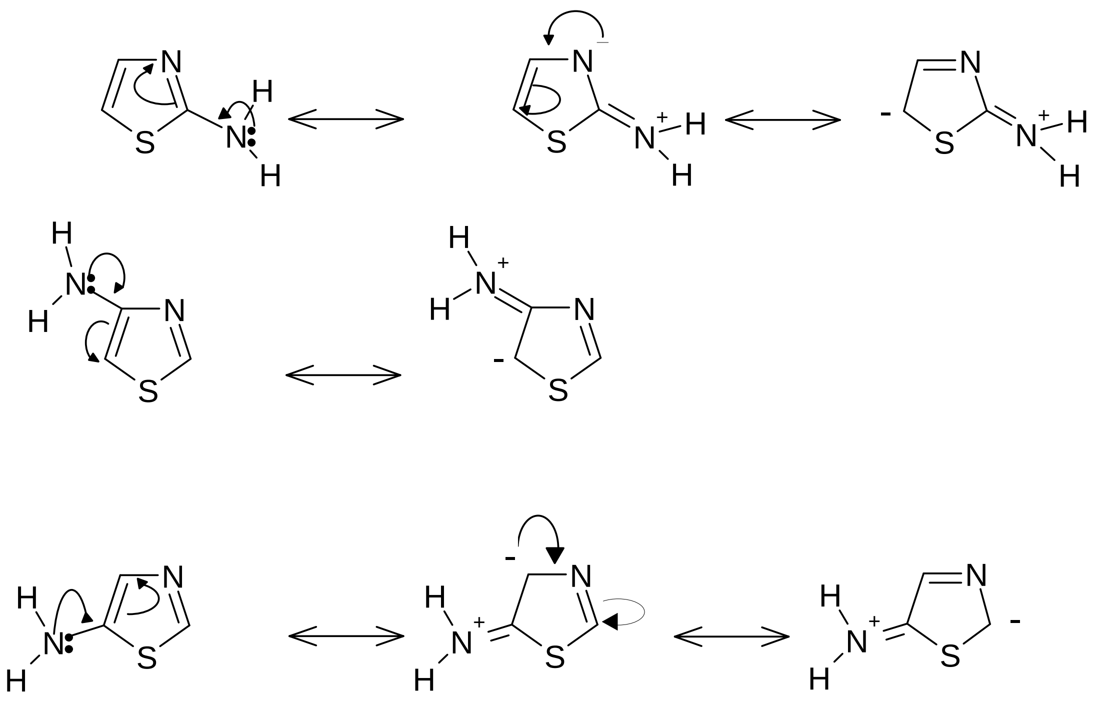
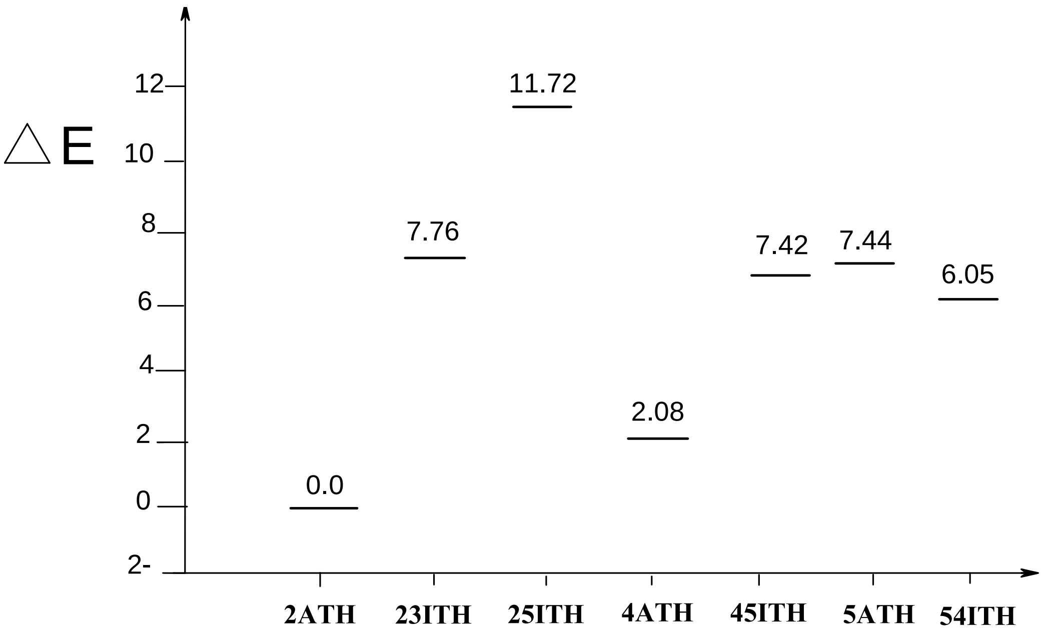
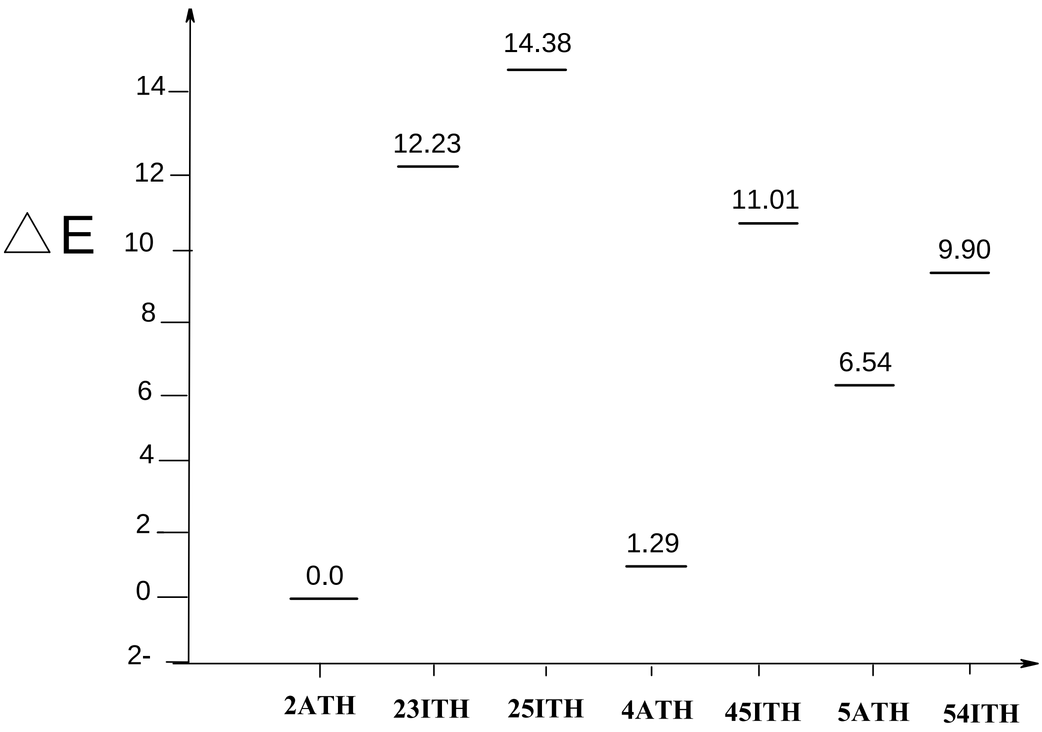


Fig. (2): Relative stabilities of **2ATH**, **4ATH** and **5ATH** tautomers calculated at the **B3LYP (A)** and **MP2 (B) /6-311++G****.



(A)



(B)

The energy difference ΔE between **4ATH** and its imino **45ITH** tautomer is 7.42 and 11.01 Kcal/mol at the B3LYP and MP2 6-311++G** levels, while the reaction enthalpy ΔH is 7.33 and 11.10 Kcal/mol, respectively. For **2ATH** isomer, the value of reaction enthalpy ΔH is 7.23 and 10.10 Kcal/mol, respectively at the same levels. The TS located has energy of 0.11426 a.u. and 0.10243 a.u. higher than the **4ATH** and its imino tautomer at the B3LYP level, leading to an activation energy of 64.14 and 67.55 Kcal/mol at the two levels. Such high values of the thermodynamic parameters of this tautomerism support the existence of only **4ATH** form. The calculated free energy ΔG and equilibrium constant K_T are 7.17 Kcal/mol and 1.82×10^5 at B3LYP level and 10.47 Kcal/mol and 4.70×10^7 at MP2 level. The energy difference ΔE and the reaction enthalpy ΔH of **5ATH** tautomerization is the least one of the series at both levels 6.05, 5.60, and 9.90, 8.60 Kcal/mol, respectively. The tautomerization constant K in this case is 9.07×10^3 at the B3LYP method and 1.03×10^7 at the MP2 method.

Comparing between the results of the three aminothiazoles isomers **2ATH**, **4ATH** and **5ATH** collected in Table (9), one can notice that:

(1) In the three isomers, the amino form is the predominant form as indicated by the values of ΔG and K_T parameters.

(2) The tautomerization activating energy of **2ATH** $\rightleftharpoons$ **23ITH** is

lower than that of **4ATH** and **5ATH** where the difference is around 17.50 and 19.32 Kcal/mol, respectively calculated at the B3LYP level.

(3) The enthalpy value (ΔH) for the two isomers **2ATH** and **4ATH** are comparable ≈ 7.3 Kcal/mol. The same trend is found also for the free energy change ΔG.

(4) The IP of **2ATH** and **5ATH** are higher than that of **4ATH**. The electron affinity of **2ATH** and **4ATH** are nearly equal and are greater than that of **5ATH**.

(5) The chemical reactivity of **2ATH** is thought to be more less than those of **4ATH** and **5ATH** according to their ΔE_g values see Tables (7 and 8).

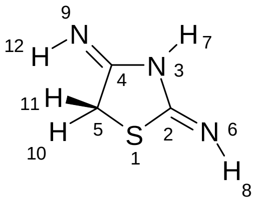
4.2. DIAMINOTHIAZOLES

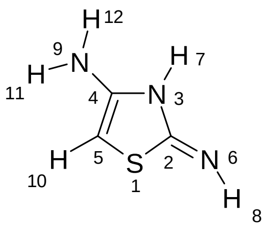
4.2.1. *GEOMETRY*

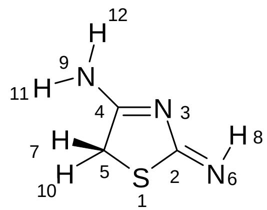
4.2.1.1. 2,4-DIAMINOTHIAZOLE AND 2,5-DIAMINO-THIAZOLE.

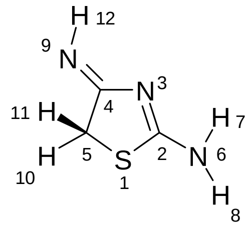
2,4-Diaminothiazole can exist in five forms as follows; 2,4-diaminothiazole **24ATH**, 4-aminothiazole-2(3H)-imino **3I4ATH**, 4-aminothiazole-2(5H)-imino **5I4ATH**, 2-aminothiazole-4(5H)-imino **2A5ITH** and thiazole-2(3H),4(5H)-diimino **3I5ITH**, Fig. (3). The calculations were performed using both B3LYP and MP2 methods with 6-311++G** basis set. The five structures represent stationary point minimum on the potential energy surface. The geometrical parameters of the most stable conformers of the above forms are collected in Tables (10-13). The data presented in these tables shows that the presence of two amino groups that remarkably affect the two C-S bonds and C_5-C_4 bond. The C-S bond elongates by 0.02Å comparing to **4ATH** but shortens by 0.01Å with respect to **2ATH** while C_5-C_4 bond elongates by 0.009Å and decreases by 0.01Å with respect to **4ATH**. The other bonds are not much affected by the second $-NH_2$ group. The lone pair of endocyclic nitrogen atom N_3 is less participated in resonance in case of diamino **24ATH** than in the two aminothiazoles **2ATH** and **4ATH**.

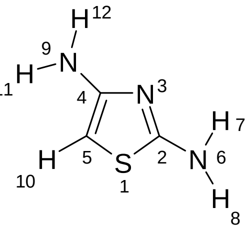
Fig(3): Structure and numbering system of 2,4-diaminothiazole (**24ATH**), 2,5-diaminothiazole, (**25ATH**) and their tautomers.

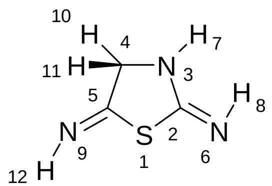

Thiazole-2(3H),4(5H)-diimino
3I5ITH

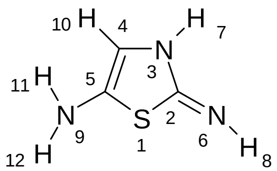

4-Aminothiazole-2(3H)-imino
3I4ATH

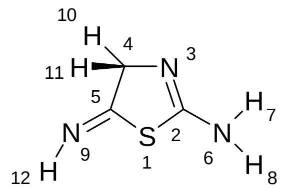

4-Aminothiazole-2(5H)-imino
5I4ATH


2-Aminothiazole-4(5H)-imino
2A5ITH


2,4-Diaminothiazole
24ATH


Thiazole-2(3H),5(4H)-diimino
3I4ITH


5-Aminothiazole-2(3H)-imino
3I5ATH


2-Aminothiazole-5(4H)-imino
2A4ITH

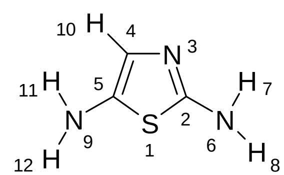

2,5-Diaminothiazole
25ATH

Table (10): Geometrical parameters of the two isomers (**24ATH** and **3I4ATH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

	MP2 6-311++G**			**B3LYP** 6-311++G**		
Bond Length Å *Bond Order*						
S_1C_2	1.733	(1.777)[a]	[1.723][b]	1.758	(1.802)a	[1.740]b
	0.979	*(0.855)*	*[1.032]*	*1.014*	*(0.900)*	*[1.084]*
S_1C_5	1.727	(1.755)	[1.752]	1.756	(1.775)	[1.783]
	0.850	*(0.691)*	*[0.777]*	*0.833*	*(0.719)*	*[0.759]*
C_2N_3	1.309	(1.389)	[1.347]	1.299	(1.388)	[1.346]
	1.536	*(1.026)*	*[1.110]*	*1.651*	*(1.105)*	*[1.193]*
N_3C_4	1.377	(1.389)	[1.377]	1.381	(1.390)	[1.376]
	0.923	*(0.820)*	*[0.936]*	*0.973*	*(0.899)*	*[1.018]*
C_4C_5	1.372	(1.352)	[1.370]	1.365	(1.346)	[1.365]
	1.747	*(1.853)*	*[1.780]*	*1.824*	*(1.897)*	*[1.800]*
C_2N_6	1.389	(1.283)	[1.335]	1.376	(1.272)	[1.321]
	1.097	*(1.789)*	*[1.296]*	*1.197*	*(1.934)*	*[1.373]*
N_6H_7	1.013	(2.561)	[1.433]	1.011	(2.573)	[1.414]
	0.910	---	*[0.383]*	*0.935*	---	*[0.400]*
N_3H_7	2.486	(1.013)	[1.290]	2.521	(1.010)	[1.318]
	---	*(0.861)*	*[0.490]*	---	*(0.895)*	*[0.494]*
C_4N_9	1.4	(1.402)	[1.396]	1.392	(1.398)	[1.389]
	0.956	*(0.853)*	*[0.955]*	*1.071*	*(0.968)*	*[1.061]*
N_9H_{11}	1.012	(1.013)	[1.012]	1.009	(1.011)	[1.009]
	0.904	*(0.886)*	*[0.872]*	*0.911*	*(0.917)*	*[0.903]*
Bond Angle **degree**						
$N_3C_2S_1$	115.4	(107.7)	[112.5]	115.1	(107.0)	[112.5]
$C_4N_3C_2$	110.2	(115.6)	[113.6]	111.0	(116.8)	[114.2]
$C_5C_4N_3$	115.7	(113.5)	[112.6]	116.1	(113.8)	[113.4]
$N_6C_2S_1$	121.4	(130.4)	[140.1]	121.4	(130.3)	[141.3]
$H_7N_6C_2$	110.8	(117.2)	[76.9]	113.7	(118.5)	[76.9]
$N_9C_4N_3$	117.1	(116.3)	[118.7]	116.7	(116.6)	[118.6]
$H_{11}N_9C_4$	113.3	(111.6)	[112.8]	115.4	(112.8)	[114.7]
Dihedral Angle **degree**						
$N_3C_2S_1N_6$	173.6	(179.3)	[166.6]	176.4	(179.1)	[175.3]
$C_4N_3C_2N_6$	174.2	(-7.4)	[163.4]	176.5	(-2.3)	[173.6]
$C_5C_4N_3C_2$	0.1	(6.4)	[6.8]	0.1	(2.8)	[2.4]
$N_6C_2S_1N_3$	173.6	(179.3)	[166.6]	176.4	(179.1)	[175.3]
$H_7N_6C_2N_3$	18.4	(19.8)	[-2.7]	17.2	(13.8)	[1.7]
$N_9C_4N_3C_2$	175.0	(-171.4)	[178.6]	176.9	(-175.0)	[178.2]
$H_{11}N_9C_4C_5$	-31.6	(0.3)	[-26.8]	-26.8	(0.4)	[-21.9]

( )[a]: correspond to imino, [ ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (11): Geometrical parameters of the two isomers (**24ATH** and **2A5ITH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

	MP2 / 6-311++G**			B3LYP / 6-311++G**		
Bond Length Å ***Bond Order***						
S_1C_2	1.733	(1.771)[a]	[1.760][b]	1.758	(1.791)a	[1.785]b
	0.979	*(0.854)*	*[0.958]*	*1.014*	*(0.881)*	*[0.995]*
S_1C_5	1.727	(1.809)	[1.792]	1.756	(1.830)	[1.825]
	0.850	*(0.730)*	*[0.825]*	*0.833*	*(0.824)*	*[0.885]*
C_2N_3	1.309	(1.294)	[1.319]	1.299	(1.289)	[1.316]
	1.536	*(1.481)*	*[1.395]*	*1.651*	*(1.575)*	*[1.451]*
N_3C_4	1.377	(1.404)	[1.364]	1.381	(1.395)	[1.356]
	0.923	*(0.942)*	*[1.052]*	*0.973*	*(1.004)*	*[1.168]*
C_4C_5	1.372	(1.525)	[1.457]	1.365	(1.537)	[1.466]
	1.747	*(0.760)*	*[1.041]*	*1.824*	*(0.836)*	*[1.142]*
C_2N_6	1.389	(1.361)	[1.359]	1.376	(1.351)	[1.345]
	1.097	*(1.158)*	*[1.146]*	*1.197*	*(1.252)*	*[1.219]*
N_6H_7	1.013	(1.011)	[1.010]	1.011	(1.008)	[1.008]
	0.910	*(0.886)*	*[0.881]*	*0.935*	*(0.910)*	*[0.902]*
C_4N_9	1.400	(1.278)	[1.320]	1.392	(1.270)	[1.314]
	0.956	*(1.828)*	*[1.435]*	*1.071*	*(1.984)*	*[1.545]*
N_9H_{11}	1.012	(2.885)	[1.314]	1.009	(2.763)	[1.328]
	0.904	---	*[0.426]*	*0.911*	---	*[0.439]*
C_5H_{11}	2.686	(1.092)	[1.497]	2.693	(1.089)	[1.497]
	---	*(0.950)*	*[0.415]*	---	*(0.983)*	*[0.423]*
Bond Angle **degree**						
$N_3C_2S_1$	115.4	(122.9)	[121.1]	115.1	(123.3)	[121.8]
$C_4N_3C_2$	110.2	(110.6)	[106.2]	111.0	(112.8)	[107.8]
$C_5C_4N_3$	115.7	(120.2)	[106.4]	116.1	(119.1)	[105.7]
$N_6C_2S_1$	121.4	(117.9)	[119.9]	121.4	(118.2)	[120.3]
$H_7N_6C_2$	110.8	(114.8)	[115.3]	113.7	(117.7)	[118.8]
$N_9C_4N_3$	117.1	(126.5)	[132.2]	116.7	(126.9)	[132.8]
$H_{11}N_9C_4$	113.3	(109.7)	[79.2]	115.4	(110.5)	[80.1]
Dihedral Angle **degree**						
$N_3C_2S_1N_6$	173.6	(-175.6)	[172.2]	176.4	(-178.4)	[175.2]
$C_4N_3C_2N_6$	174.2	(173.6)	[-169.4]	176.5	(178.3)	[-173.5]
$C_5C_4N_3C_2$	0.1	(178.8)	[168.9]	0.1	(179.8)	[169.9]
$N_6C_2S_1N_3$	173.6	(-175.6)	[172.2]	176.4	(-178.4)	[175.2]
$H_7N_6C_2N_3$	18.4	(13.8)	[-13.8]	17.2	(8.3)	[0.5]
$N_9C_4N_3C_2$	175.0	(-166.8)	[153.1]	176.9	(-179.2)	[155.6]
$H_{11}N_9C_4C_5$	-31.6	(-80.3)	[-162.8]	-26.8	(-61.7)	[-162.3]

( )[a]: correspond to imino, [ ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (12): Geometrical parameters of the two isomers (**24ATH** and **5I4ATH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

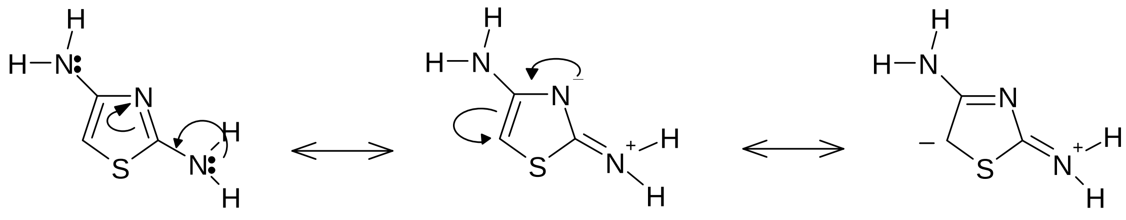
	MP2 / 6-311++G**			**B3LYP / 6-311++G****		
Bond Length Å *Bond Order*						
S_1C_2	1.733	(1.791)[a]	[1.786][b]	1.758	(1.820)a	[1.817]b
	0.979	*(0.752)*	*[1.020]*	*1.014*	*(0.816)*	*[1.032]*
S_1C_5	1.727	(1.803)	[1.775]	1.756	(1.821)	[1.841]
	0.850	*(0.761)*	*[0.793]*	*0.833*	*(0.825)*	*[0.807]*
C_2N_3	1.309	(1.407)	[1.389]	1.299	(1.397)	[1.362]
	1.536	*(0.991)*	*[0.887]*	*1.651*	*(1.100)*	*[1.094]*
N_3C_4	1.377	(1.291)	[1.314]	1.381	(1.288)	[1.329]
	0.923	*(1.430)*	*[1.463]*	*0.973*	*(1.492)*	*[1.442]*
C_4C_5	1.372	(1.512)	[1.461]	1.365	(1.518)	[1.459]
	1.747	*(0.866)*	*[1.200]*	*1.824*	*(0.930)*	*[1.273]*
C_2N_6	1.389	(1.275)	[1.349]	1.376	(1.264)	[1.329]
	1.097	*(1.898)*	*[1.404]*	*1.197*	*(2.073)*	*[1.549]*
N_6H_7	1.013	(4.506)	[1.321]	1.011	(4.532)	[1.343]
	0.910	---	*[0.507]*	*0.935*	---	*[0.511]*
C_5H_7	4.377	(1.093)	[1.707]	4.422	(1.093)	[1.728]
	---	*(0.937)*	*[0.485]*	---	*(0.970)*	*[0.473]*
C_4N_9	1.400	(1.363)	[1.377]	1.392	(1.354)	[1.358]
	0.956	*(1.064)*	*[1.070]*	*1.071*	*(1.161)*	*[1.187]*
N_9H_{11}	1.012	(1.008)	[1.010]	1.009	(1.005)	[1.006]
	0.904	*(0.854)*	*[0.866]*	0.911	(0.885)	[0.890]
Bond Angle degree						
$N_3C_2S_1$	115.4	(113.1)	[114.2]	115.1	(112.3)	[113.9]
$C_4N_3C_2$	110.2	(111.7)	[103.2]	111.0	(113.2)	[102.5]
$C_5C_4N_3$	115.7	(119.8)	[115.1]	116.1	(119.6)	[114.8]
$N_6C_2S_1$	121.4	(120.1)	[104.2]	121.4	(119.6)	[107.8]
$H_7N_6C_2$	110.8	(109.5)	[90.6]	113.7	(110.5)	[93.3]
$N_9C_4N_3$	117.1	(122.1)	[122.4]	116.7	(122.0)	[121.2]
$H_{11}N_9C_4$	113.3	(117.8)	[115.8]	115.4	(121.1)	[119.7]
Dihedral Angle degree						
$N_3C_2S_1N_6$	173.6	(179.7)	[127.3]	176.4	(179.9)	[136.5]
$C_4N_3C_2N_6$	174.2	(0.8)	[87.7]	176.5	(0.3)	[92.4]
$C_5C_4N_3C_2$	0.1	(0.0)	[1.1]	0.1	(0.1)	[1.3]
$N_6C_2S_1N_3$	173.6	(179.7)	[127.3]	176.4	(179.9)	[136.5]
$H_7N_6C_2N_3$	18.4	(119.2)	[-21.7]	17.2	(119.8)	[-19.9]
$N_9C_4N_3C_2$	175.0	(175.7)	[-169.9]	176.9	(178.4)	[-171.8]
$H_{11}N_9C_4C_5$	-31.6	(159.0)	[47.9]	-26.8	(170.9)	[30.9]

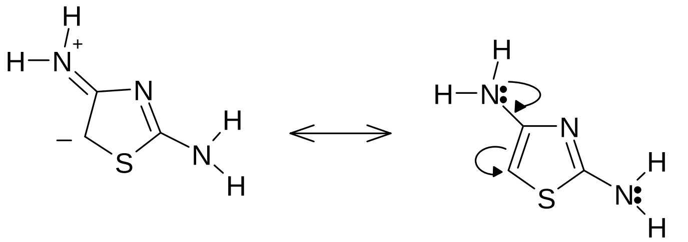
(   )[a]: correspond to imino, [   ][b]: correspond to TS
Values in italic refer to **Bond Order**.

Table (13): Geometrical parameters of the two isomers (**24ATH** and **3I5ITH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

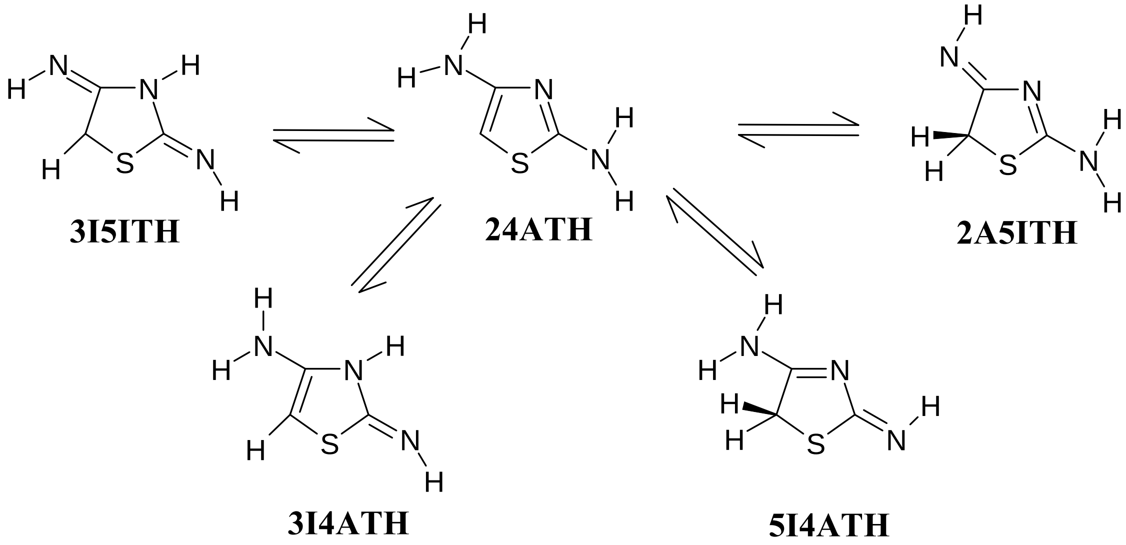
	MP2 / 6-311++G**		**B3LYP / 6-311++G****	
Bond Length Å *Bond Order*				
S_1C_2	1.733	(1.781)[a]	1.758	(1.803)[a]
	0.979	*(0.798)*	*1.014*	*(0.850)*
S_1C_5	1.727	(1.817)	1.756	(1.837)
	0.850	*(0.798)*	*0.833*	*(0.865)*
C_2N_3	1.309	(1.387)	1.299	(1.383)
	1.536	*(0.951)*	*1.651*	*(1.031)*
N_3C_4	1.377	(1.382)	1.381	(1.378)
	0.923	*(0.865)*	*0.973*	*(0.931)*
C_4C_5	1.372	(1.517)	1.365	(1.525)
	1.747	*(0.777)*	*1.824*	*(0.800)*
C_2N_6	1.389	(1.276)	1.376	(1.265)
	1.097	*(1.835)*	*1.197*	*(1.958)*
N_6H_7	1.013	(2.547)	1.011	(2.561)
	0.910	---	*0.935*	---
N_3H_7	2.486	(1.014)	2.467	(1.011)
	---	*(0.868)*	---	*(0.895)*
C_4N_9	1.400	(1.279)	1.392	(1.271)
	0.956	*(1.815)*	*1.071*	*(1.916)*
N_9H_{11}	1.012	(2.791)	1.010	(2.865)
	0.904	---	*0.937*	---
C_5H_{11}	2.686	(1.091)	2.693	(1.090)
	---	*(0.973)*	---	*(0.984)*
Bond Angle degree				
$N_3C_2S_1$	115.4	(109.3)	115.1	(108.9)
$C_4N_3C_2$	110.2	(117.8)	111.0	(120.6)
$C_5C_4N_3$	115.7	(129.0)	116.1	(127.8)
$N_6C_2S_1$	121.4	(128.9)	121.4	(128.7)
$H_7N_6C_2$	110.8	(117.6)	113.7	(119.1)
$N_9C_4N_3$	117.1	(121.7)	116.7	(121.6)
$H_{11}N_9C_4$	113.3	(110.5)	115.4	(110.0)
Dihedral Angle degree				
$N_3C_2S_1N_6$	173.6	(179.5)	176.4	(180.0)
$C_4N_3C_2N_6$	174.2	(10.9)	176.5	(0.0)
$C_5C_4N_3C_2$	0.1	(-176.3)	0.1	(180.0)
$N_6C_2S_1N_3$	173.6	(179.5)	176.4	(180.0)
$H_7N_6C_2N_3$	18.4	(-14.1)	17.2	(0.0)
$N_9C_4N_3C_2$	175.0	(160.2)	176.9	(180.0)
$H_{11}N_9C_4C_5$	-31.6	(143.3)	-26.8	(119.8)

(   )[a]: correspond to imino and values in italic refer to **Bond Order**.





This is reflected on the values of bond lengths N_3C_4, C_2S_1 and C_4C_5 where they have more single character (the first one) or more double bond character for the latter. The differences in bond length between the imino forms (**2A5ITH**, **3I4ATH** and **5I4ATH**) comparing to the corresponding mono imino compounds (**4ITH**, **3ITH** and **5ITH**) is attributed to the extent of involvement of N_3 lone pair in resonance. The first group has more conjugation, this can be easily noticed through the comparison between the same bond lengths and bond order values of thiazole ring in the two series. On the other hand, the least conjugation is found in case of **3I5ITH** conformer, pure single, and double bond lengths because N_3 lone pair participates in resonance with the two exo amino groups. Structure **3I4ATH** has the most conjugation of N_3 lone pair with $C_2{=}N_6$ bond comparing to **3I5ITH** and **5I4ATH**, where C_2-N_6 bond length is 1.272, 1.265 and 1.264 Å at the three forms, respectively.



To elucidate the effect of position of the second substituent $-NH_2$ group on structural properties and tautomeric process of diaminothiazole, the compound 2,5-diaminothiazole **25ATH** is studied, the results are depicted in Tables (14-16). The presence of the second $-NH_2$ group in position five of the ring changes the geometrical parameters of **2ATH**. **25ATH** has longer C_2S_1, C_5S_1, C_4C_5 and C_2N_6 bonds than **2ATH** or **24ATH** while C_2N_3 is shorter, Table (17). This means that 5-NH_2 group decreases the extent of delocalization over the thiazole ring. The same trends were found in case of 5-aminothiazole-2(3H)-imino **3I5ATH** comparing to **3I4ATH** isomers.

Table (14): Geometrical parameters of the two isomers (**25ATH** and **3I5ATH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

	MP2 6-311++G**			B3LYP 6-311++G**		
Bond Length Å *Bond Order*						
S_1C_2	1.744	(1.783)[a]	[1.730][b]	1.771	(1.812)[a]	[1.740][b]
	0.921	*(0.834)*	*[0.967]*	*0.957*	*(0.864)*	*[1.031]*
S_1C_5	1.741	(1.763)	[1.768]	1.771	(1.786)	[1.816]
	0.892	*(0.828)*	*[0.856]*	*0.878*	*(0.891)*	*[0.821]*
C_2N_3	1.307	(1.382)	[1.346]	1.293	(1.378)	[1.346]
	1.620	*(1.039)*	*[1.225]*	*1.765*	*(1.179)*	*[1.305]*
N_3C_4	1.378	(1.395)	[1.379]	1.383	(1.396)	[1.373]
	0.873	*(0.804)*	*[0.901]*	*0.904*	*(0.864)*	*[0.993]*
C_4C_5	1.373	(1.353)	[1.371]	1.359	(1.343)	[1.359]
	1.674	*(1.908)*	*[1.708]*	*1.844*	*(2.024)*	*[1.850]*
C_2N_6	1.393	(1.284)	[1.338]	1.383	(1.273)	[1.323]
	1.065	*(1.739)*	*[1.308]*	*1.159*	*(1.886)*	*[1.367]*
N_6H_7	1.014	(2.542)	[1.435]	1.012	(2.572)	[1.414]
	0.909	---	*[0.391]*	*0.936*	---	*[0.409]*
N_3H_7	2.474	(1.011)	[1.292]	2.509	(1.008)	[1.322]
	---	*(0.868)*	*[0.487]*	---	*(0.898)*	*[0.496]*
C_5N_9	1.405	(1.404)	[1.404]	1.401	(1.400)	[1.398]
	1.103	*(1.080)*	*[1.149]*	*1.215*	*(1.169)*	*[1.355]*
N_9H_{11}	1.013	(1.013)	[1.012]	1.012	(1.012)	[1.010]
	0.916	*(0.912)*	*[0.912]*	*0.954*	*(0.950)*	*[0.934]*
Bond Angle degree						
$N_3C_2S_1$	115.4	(107.3)	[112.4]	114.9	(106.6)	[112.4]
$C_4N_3C_2$	110.2	(115.6)	[113.5]	111.2	(117.1)	[114.1]
$C_5C_4N_3$	116.3	(113.5)	[113.2]	116.9	(114.3)	[114.9]
$N_6C_2S_1$	129.5	(130.2)	[139.5]	120.5	(129.8)	[141.1]
$H_7N_6C_2$	109.9	(116.6)	[76.7]	112.3	(118.7)	[76.8]
$N_9C_5C_4$	129.8	(129.6)	[129.8]	130.9	(130.4)	[132.0]
$H_{11}N_9C_5$	111.2	(111.8)	[112.3]	112.7	(113.2)	[115.5]
Dihedral Angle degree						
$N_3C_2S_1N_6$	172.2	(179.9)	[164.4]	174.8	(-179.9)	[172.4]
$C_4N_3C_2N_6$	171.3	(167.2)	[159.5]	173.1	(175.3)	[169.3]
$C_5C_4N_3C_2$	0.3	(9.8)	[8.1]	1.2	(3.8)	[4.8]
$N_6C_2S_1N_3$	172.2	(179.9)	[164.4]	174.8	(179.9)	[172.4]
$H_7N_6C_2N_3$	12.3	(13.0)	[-2.9]	12.4	(3.0)	[-1.9]
$N_9C_5C_4N_3$	170.9	(168.8)	[166.9]	172.5	(172.4)	[173.0]
$H_{11}N_9C_5C_4$	-7.4	(-5.5)	[-19.1]	-11.2	(-8.3)	[-47.8]

( )[a]: correspond to imino, [ ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (15): Geometrical parameters of the two isomers (**25ATH** and **2A4ITH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

	MP2 / 6-311++G**			B3LYP / 6-311++G**		
Bond Length Å *Bond Order*						
S_1C_2	1.744	(1.788)[a]	[1.809][b]	1.771	(1.812)[a]	[1.851][b]
	0.921	*(0.807)*	*[0.842]*	*0.957*	*(0.852)*	*[0.866]*
S_1C_5	1.741	(1.786)	[1.737]	1.771	(1.811)	[1.752]
	0.892	*(0.813)*	*[1.017]*	*0.878*	*(0.877)*	*[1.088]*
C_2N_3	1.307	(1.280)	[1.289]	1.293	(1.268)	[1.271]
	1.620	*(1.682)*	*[1.626]*	*1.765*	*(1.812)*	*[1.790]*
N_3C_4	1.378	(1.449)	[1.417]	1.383	(1.444)	[1.420]
	0.873	*(0.812)*	*[0.879]*	*0.904*	*(0.920)*	*[0.950]*
C_4C_5	1.373	(1.522)	[1.434]	1.359	(1.532)	[1.438]
	1.674	*(0.854)*	*[0.957]*	*1.844*	*(0.924)*	*[1.049]*
C_2N_6	1.393	(1.378)	[1.385]	1.383	(1.371)	[1.379]
	1.065	*(1.107)*	*[1.102]*	*1.159*	*(1.199)*	*[1.189]*
N_6H_7	1.014	(1.013)	[1.014]	1.012	(1.011)	[1.012]
	0.909	*(0.895)*	*[0.900]*	*0.936*	*(0.926)*	*[0.931]*
C_5N_9	1.405	(1.273)	[1.330]	1.401	(1.260)	[1.317]
	1.103	*(1.985)*	*[1.449]*	*1.215*	*(2.179)*	*[1.559]*
N_9H_{11}	1.013	(2.666)	[1.362]	1.012	(2.744)	[1.361]
	0.916	----	*[0.839]*	*0.954*	---	*[0.405]*
C_4H_{11}	2.656	(1.092)	[1.497]	2.690	(1.094)	[1.524]
	---	*(0.978)*	*[0.456]*	---	*(0.968)*	*[0.469]*
Bond Angle degree						
$N_3C_2S_1$	115.4	(118.8)	[118.0]	114.9	(118.0)	[116.7]
$C_4N_3C_2$	110.2	(111.4)	[110.1]	111.2	(113.5)	[112.0]
$C_5C_4N_3$	116.3	(110.6)	[112.0]	116.9	(111.6)	[111.8]
$N_6C_2S_1$	129.5	(116.8)	[116.4]	120.5	(116.8)	[116.3]
$H_7N_6C_2$	109.9	(112.2)	[110.9]	112.3	(114.5)	[112.9]
$N_9C_5C_4$	129.8	(122.8)	[109.1]	130.9	(123.3)	[109.4]
$H_{11}N_9C_5$	111.2	(111.1)	[69.6]	112.7	(110.7)	[69.4]
Dihedral Angle degree						
$N_3C_2S_1N_6$	172.2	(176.2)	[176.1]	174.8	(177.1)	[177.5]
$C_4N_3C_2N_6$	171.3	(173.0)	[1.0]	173.1	(175.7)	[1.5]
$C_5C_4N_3C_2$	0.3	(14.1)	[10.1]	1.2	(3.4)	[9.7]
$N_6C_2S_1N_3$	172.2	(176.2)	[176.1]	174.8	(177.1)	[177.5]
$H_7N_6C_2N_3$	12.3	(14.1)	[11.7]	12.4	(13.5)	[11.6]
$N_9C_5C_4N_3$	170.9	(161.4)	[150.8]	172.5	(176.4)	[153.5]
$H_{11}N_9C_5C_4$	-7.4	(135.7)	[5.7]	-11.2	(124.6)	[6.7]

(   )[a]: correspond to imino, [   ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (16): Geometrical parameters of the two isomers (**25ATH** and **3I4ITH**) calculated at the **MP2** and the **B3LYP /6-311++G****.

	MP2 6-311++G**		B3LYP 6-311++G**	
Bond Length Å *Bond Order*				
S_1C_2	1.744	(1.779)[a]	1.771	(1.801)[a]
	0.921	*(0.853)*	*0.957*	*(0.884)*
S_1C_5	1.741	(1.771)	1.771	(1.791)
	0.892	*(0.821)*	*0.878*	*(0.879)*
C_2N_3	1.307	(1.391)	1.293	(1.380)
	1.620	*(1.086)*	*1.765*	*(1.148)*
N_3C_4	1.378	(1.456)	1.383	(1.454)
	0.873	*(0.681)*	*0.904*	*(0.772)*
C_4C_5	1.373	(1.512)	1.359	(1.520)
	1.674	*(0.856)*	*1.844*	*(0.934)*
C_2N_6	1.393	(1.277)	1.383	(1.267)
	1.065	*(1.947)*	*1.159*	*(2.103)*
N_6H_7	1.014	(2.661)	1.012	(2.687)
	0.909	---	*0.936*	---
N_3H_7	2.474	(1.014)	2.474	(1.010)
	---	*(0.877)*	---	*(0.906)*
C_5N_9	1.405	(1.275)	1.401	(1.263)
	1.103	*(1.922)*	*1.215*	*(2.108)*
N_9H_{11}	1.013	(2.621)	1.012	(2.674)
	0.916	---	*0.954*	---
C_4H_{11}	2.656	(1.091)	2.690	(1.092)
	---	*(0.975)*	---	*(0.985)*
Bond Angle degree				
$N_3C_2S_1$	115.4	(109.8)	114.9	(109.2)
$C_4N_3C_2$	110.2	(114.8)	111.2	(118.3)
$C_5C_4N_3$	116.3	(106.0)	116.9	(107.5)
$N_6C_2S_1$	129.5	(119.7)	120.5	(119.6)
$H_7N_6C_2$	109.9	(114.0)	112.3	(117.1)
$N_9C_5C_4$	129.8	(121.2)	130.9	(121.3)
$H_{11}N_9C_5$	111.2	(111.4)	112.7	(111.6)
Dihedral Angle degree				
$N_3C_2S_1N_6$	172.2	(-177.3)	174.8	(-178.2)
$C_4N_3C_2N_6$	171.3	(161.4)	173.1	(169.2)
$C_5C_4N_3C_2$	0.3	(30.1)	1.2	(16.3)
$N_6C_2S_1N_3$	172.2	(-177.3)	174.8	(-178.2)
$H_7N_6C_2N_3$	12.3	(23.7)	12.4	(16.1)
$N_9C_5C_4N_3$	170.9	(156.3)	172.5	(169.3)
$H_{11}N_9C_5C_4$	-7.4	(149.1)	-11.2	(135.7)

( )[a]: correspond to imino, [ ][b]: correspond to TS.
Values in italic refer to **Bond Order**.

Table (17): Comparing geometrical parameters of **24ATH**, **25ATH** and their tautomers calculated at the **B3LYP** and **MP2** / **6-311++G****.

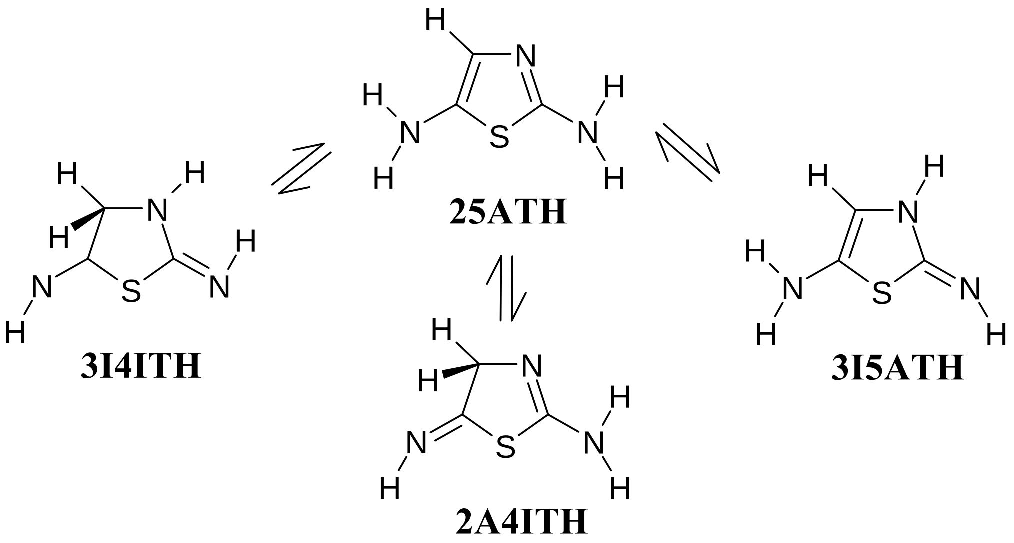
Bond Length Å	S_1C_2	S_1C_5	C_2N_3	N_3C_4	C_4C_5	C_2N_6	CN_9	N_6H_7	N_9H
24ATH	1.758	1.756	1.299	1.381	1.365	1.376	1.392	1.011	1.009
1	*1.733*	*1.727*	*1.309*	*1.377*	*1.372*	*1.389*	*1.400*	*1.013*	*1.012*
25ATH	1.771	1.771	1.293	1.383	1.359	1.383	1.401	1.012	1.012
2	*1.744*	*1.741*	*1.307*	*1.378*	*1.373*	*1.393*	*1.405*	*1.014*	*1.013*
3I4ATH	1.802	1.775	1.388	1.390	1.346	1.272	1.398	2.573	1.011
1.1	*1.777*	*1.755*	*1.389*	*1.389*	*1.352*	*1.283*	*1.402*	*2.561*	*1.013*
2A5ITH	1.791	1.830	1.289	1.395	1.537	1.351	1.270	1.008	2.763
1.2	*1.771*	*1.809*	*1.294*	*1.404*	*1.525*	*1.361*	*1.278*	*1.011*	*2.885*
5I4ATH	1.820	1.821	1.397	1.288	1.518	1.264	1.354	4.532	1.005
1.3	*1.791*	*1.803*	*1.407*	*1.291*	*1.512*	*1.275*	*1.363*	*4.506*	*1.008*
3I5ITH	1.803	1.837	1.383	1.378	1.525	1.265	1.271	2.561	2.865
1.4	*1.781*	*1.817*	*1.387*	*1.382*	*1.517*	*1.276*	*1.279*	*2.547*	*2.791*
3I5ATH	1.812	1.786	1.378	1.396	1.343	1.273	1.400	2.572	1.012
2.1	*1.783*	*1.763*	*1.382*	*1.395*	*1.353*	*1.284*	*1.404*	*2.542*	*1.013*
2A4ITH	1.812	1.811	1.268	1.444	1.532	1.371	1.260	1.011	2.744
2.2	*1.788*	*1.786*	*1.280*	*1.449*	*1.522*	*1.378*	*1.273*	*1.013*	*2.666*
3I4ITH	1.801	1.791	1.380	1.454	1.520	1.267	1.263	2.687	2.674
2.3	*1.779*	*1.771*	*1.391*	*1.456*	*1.512*	*1.277*	*1.275*	*2.661*	*2.621*
TS_1	1.740	1.783	1.346	1.376	1.365	1.321	1.389	1.414	1.009
1.1	*1.723*	*1.752*	*1.347*	*1.377*	*1.370*	*1.335*	*1.396*	*1.433*	*1.012*
TS_2	1.785	1.825	1.316	1.356	1.466	1.345	1.314	1.008	1.328
1.2	*1.760*	*1.792*	*1.319*	*1.364*	*1.457*	*1.359*	*1.320*	*1.010*	*1.314*
TS_3	1.817	1.841	1.362	1.329	1.459	1.329	1.358	1.343	1.006
1.3	*1.786*	*1.775*	*1.389*	*1.314*	*1.461*	*1.349*	*1.377*	*1.321*	*1.010*
TS_5	1.740	1.816	1.346	1.373	1.359	1.323	1.398	1.414	1.010
2.1	*1.730*	*1.768*	*1.346*	*1.379*	*1.371*	*1.338*	*1.404*	*1.435*	*1.012*
TS_6	1.851	1.752	1.271	1.420	1.438	1.379	1.317	1.012	1.361
2.2	*1.809*	*1.737*	*1.289*	*1.417*	*1.434*	*1.385*	*1.330*	*1.014*	*1.362*

Values in italic refer to **MP2**.

Table (17): Continue.

Bond Angle degree	**24ATH 1**	**25ATH 2**	**3I4ATH 1.1**	**2A5ITH 1.2**	**5I4ATH 1.3**	**3I5ITH 1.4**	**3I5ATH 2.1**	**2A4ITH 2.2**	**3I4ITH 2.3**	**TS_1 1.1**	**TS_2 1.2**	**TS_3 1.3**	**TS_5 2.1**	**TS_6 2.2**
$N_3C_2S_1$	115.1 *115.4*	114.9 *115.4*	107.0 *107.7*	$N_3C_2N_6$ 123.3 *122.9*	112.3 *113.1*	108.9 *109.3*	106.6 *107.3*	118.0 *118.8*	109.2 *109.8*	112.5 *112.5*	$N_3C_2N_6$ 121.8 *121.1*	113.9 *114.2*	112.4 *112.4*	116.7 *118.0*
$C_4N_3C_2$	111.0 *110.2*	111.2 *110.2*	116.8 *115.6*	112.8 *110.6*	113.2 *111.7*	120.6 *117.8*	117.1 *115.6*	113.5 *111.4*	118.3 *114.8*	114.2 *113.6*	107.8 *106.2*	102.5 *103.2*	114.1 *113.5*	112.0 *110.1*
$C_5C_4N_3$	116.1 *115.7*	116.9 *116.3*	113.8 *113.5*	$C_5C_4N_9$ 119.1 *120.2*	119.6 *119.8*	$C_5C_4N_9$ 127.8 *129.0*	114.3 *113.5*	111.6 *110.6*	107.5 *106.0*	113.4 *112.6*	$C_5C_4N_9$ 105.7 *106.4*	114.8 *115.1*	114.9 *113.2*	111.8 *112.0*
$N_6C_2S_1$	121.4 *121.4*	120.5 *129.5*	130.3 *130.4*	118.2 *117.9*	119.6 *120.1*	128.7 *128.9*	129.8 *130.2*	116.8 *116.8*	119.6 *119.7*	141.3 *140.1*	120.3 *119.9*	107.8 *104.2*	141.1 *139.5*	116.3 *116.4*
H_7	$H_7N_6C_2$ 113.7 *110.8*	$H_7N_6C_2$ 112.3 *109.9*	$H_7N_3C_2$ 118.5 *117.2*	$H_7N_6C_2$ 117.7 *114.8*	$H_7C_5C_4$ 110.5 *109.5*	$H_7N_3C_2$ 119.1 *117.6*	$H_7N_3C_2$ 118.7 *116.6*	$H_7N_6C_2$ 114.5 *112.2*	$H_7N_3C_2$ 117.1 *114.0*	$H_7N_3C_2$ 76.9 *76.9*	$H_7N_6C_2$ 118.8 *115.3*	$H_7C_5C_4$ 93.3 *90.6*	$H_7N_3C_2$ 76.8 *76.7*	$H_7N_6C_2$ 112.9 *110.9*
N_9	$N_9C_4N_3$ 116.7 *117.1*	$N_9C_5C_4$ 130.9 *129.8*	$N_9C_4N_3$ 116.6 *116.3*	$N_9C_4N_3$ 126.9 *126.5*	$N_9C_4N_3$ 122.0 *122.1*	$N_9C_4N_3$ 121.6 *121.7*	$N_9C_5C_4$ 130.4 *129.6*	$N_9C_5C_4$ 123.3 *122.8*	$N_9C_5C_4$ 121.3 *121.2*	$N_9C_4N_3$ 118.6 *118.7*	$N_9C_4N_3$ 132.8 *132.2*	$N_9C_4N_3$ 121.2 *122.4*	$N_9C_5C_4$ 132.0 *129.8*	$N_9C_5C_4$ 109.4 *109.1*
H_{11}	$H_{11}N_9C_4$ 115.4 *113.3*	$H_{11}N_9C_5$ 112.7 *111.2*	$H_{11}N_9C_4$ 112.8 *111.6*	$H_{11}N_9C_4$ 110.5 *109.7*	$H_{11}N_9C_4$ 121.1 *117.8*	$H_{11}N_9C_4$ 110.0 *110.5*	$H_{11}N_9C_5$ 113.2 *111.8*	$H_{11}C_4N_3$ 110.7 *111.1*	$H_{11}C_4N_3$ 111.6 *111.4*	H11N9C4 114.7 *112.8*	$H_{11}N_9C_4$ 80.1 *79.2*	$H_{11}N_9C_4$ 119.7 *115.8*	$H_{11}N_9C_5$ 115.5 *112.3*	$H_{11}C_4C_5$ 69.4 *69.6*

Values in italic refer to **MP2**.



4.2.2. ***DIPOLE MOMENT***

The Mülliken atomic charge on the two exocyclic and endocyclic (more basic) nitrogen atoms increases and the positive charge on carbon atom (C_5) increases. This leads to a decrease of its dipole moment (0.566 D) and thus becomes less polar comparing to the two monosubstituted, 1.705 and 1.574 D. This is explained as the opposite directions of dipole vectors of the ring and the two amino substituents. The gas phase dipole moment values of the five tautomers of 2,4-diaminothiazole vary from 0.566 D to 6.633 D at B3LYP level, and can be arranged as follows: **24ATH < 3I5ITH < 3I4ATH < 2A5ITH < 5I4ATH**. This can be attributed to the directions of the dipole vectors of the two amino or imino groups. They are opposite in the case of **24ATH**, while for **5I4ATH**, these dipole vectors are alined. Consequently, it is expected to find a pronounced solvent effect on their equilibrium ratios in different media. The charge distribution of **24ATH** is totally changed upon change of $-NH_2$

position to **25ATH**. A negative charge is transferred and concentrated on C_2 atom. This is reflected on the dipole moment value of both compounds. The dipole moment of **25ATH** increases by ≈ 0.29 D but still less than the corresponding **2ATH** or **5ATH** i.e. the dipole vectors of the two amino groups are opposite in direction. The dipole moment of **24ATH** imino forms are higher than that of **25ATH** tautomers. On the other hand, the dipole moment of **25ATH** is less than its imino isomers as in case of **24ATH** while the dipole moment trend of the three imino isomers is (3.907 D) **3I5ATH** > (3.007 D) **3I4ITH** > (2.830 D) **2A4ITH**. (B3LYP)

4.2.3. ***IONIZATION POTENTIAL***

Tables (18 and 19) show the E_{HOMO} and E_{LUMO} for the five isomers of 2,4-diaminothiazole. The order of their IP calculated at MP2 level is

3I4ATH ≈ 24ATH < 5I4ATH ≈ 2A5ITH < 3I5ITH.

Comparing to the IP of the two monoaminothiazoles, the substitution of **2ATH** or **4ATH** by a second $-NH_2$ group destabilizes their HOMO and thus decreases the IP of **24ATH** (diamino). The E_{LUMO} of **2ATH** is not affected at MP2 by the new substitution while E_{LUMO} of **4ATH** decreases to (1.105 eV). Consequently, the order of mono and diaminothiazoles energy gap ΔE_g is; **2ATH** (9.649 eV) > **4ATH** (9.475 eV) > **24ATH** (9.007 eV) i.e. the reactivity of the diamino is higher than the reactivities of both monoaminothiazoles. The reactivity of the five tautomers of

2,4-diaminothiazole has the arrangement **3I4ATH > 24ATH > 5I4ATH > 2A5ITH > 3I5ITH**. Tables (18 and 19) show the relative values of E_{HOMO}, E_{LUMO} for **24ATH**, **25ATH** and their tautomers. The data in these Tables (18 and 19) show that:

(1) Existence of second $–NH_2$ group destabilizes the HOMO of 2-, 4- or 5- aminothiazole. This leads to lower IP values.

(2) **25ATH** also, destabilizes the LUMO of **2-** or **5-ATH**.

(3) E_{HOMO} of **25ATH** (-8.038 eV) is more stable than that **24ATH** (-7.878 eV), while the reverse order is found for E_{LUMO} (1.042 and 1.129 eV), respectively at MP2 method.

(4) The order of E_{HOMO} for each series at the MP2 level is **[**(-7.861 eV) **3I4ATH** ≈ (-7.878 eV) **24ATH** < (-9.407 eV) **5I4ATH** ≈ (-9.475 eV) **2A5ITH** < (-10.014 eV) **3I5ITH]**.

[(-7.837 eV) **3I5ATH** < (-8.038 eV) **25ATH** < (-9.679 eV) **2A4ITH** < (-9.940 eV) **3I4ITH].**

(5) The reactivity of **24ATH** is nearly equal to that of **25ATH** as indicated by ΔE_g values (9.007 and 9.080 eV).

(6) The order of energy gap ΔE_g for each series at the MP2 method is:

[(8.694 eV) **3I4ATH** < (9.007 eV) **24ATH** < (10.033 eV) **5I4ATH** < (10.381 eV) **2A5ITH** < (10.931 eV) **3I5ITH].**

[(8.656 eV) **3I5ATH** < (9.080 eV) **25ATH** < (10.686 eV) **2A4ITH** ≈ (10.778 eV) **3I4ITH].**

Table (18): Zero Point Energy **ZPE**, Thermal Correction **TC**, Ionization Potential, net charges and dipole moments in gas, water (w) and CCl_4 of **24ATH**, **25ATH** and their tautomers calculated at the **B3LYP/6-311++G****.

	24ATH 1	**25ATH 2**	**3I4ATH 1.1**	**2A5ITH 1.2**	**5I4ATH 1.3**	**3I5ITH 1.4**	**3I5ATH 2.1**	**2A4ITH 2.2**	**3I4ITH 2.3**	**TS_1 1.1**	**TS_2 1.2**	**TS_3 1.3**	**TS_5 2.1**	**TS_6 2.2**
ZPE	55.46	55.45	55.45	55.38	55.43	55.76	55.16	55.31	55.34	51.61	51.34	51.69	51.22	51.19
TC	59.79	59.85	59.71	59.69	59.69	59.84	59.58	59.57	59.54	55.92	55.59	55.59	55.18	55.28
S	81.03	81.77	80.96	82.50	81.63	81.54	82.18	81.99	82.11	81.45	81.35	78.38	79.17	79.69
E_{HOMO} eV	-5.320	-5.573	-5.377	-6.615	-6.512	-7.086	-5.331	-6.765	-7.021					
E_{LUMO} eV	-0.495	-0.536	-0.743	-0.917	-1.045	-0.846	-0.629	-0.833	-0.950					
ΔE_g eV	4.825	5.037	4.634	5.698	5.467	6.24	4.702	5.932	6.071					
IP eV	5.320	5.573	5.377	6.615	6.512	7.086	5.331	6.765	7.021					
Dipole Moment D														
D.M(gas)	0.566	0.851	3.751	4.193	6.633	3.123	3.907	2.830	3.007	1.608	3.327	3.762	2.145	2.237
D.M(W)	0.792	1.274	4.946	5.711	9.182	4.198	5.205	3.874	4.092	2.058	4.321	5.064	2.827	3.075
D.M(CCL_4)	0.649	1.006	4.276	4.813	7.683	3.544	4.467	3.196	3.444	1.801	3.737	4.298	2.447	2.549
Charge														
N_3	-0.197	-0.141	-0.134	-0.152	-0.131	-0.045	-0.107	-0.124	-0.104	-0.221	-0.163	-0.088	-0.149	-0.091
C_4	-0.480	-0.256	-0.434	-0.200	-0.052	-0.090	-0.083	-0.565	-0.440	-0.532	-0.133	-0.195	-0.252	-0.640
C_5	0.103	-0.210	0.167	-0.340	-0.380	-0.433	-0.357	-0.054	-0.109	0.113	-0.448	-0.324	-0.243	0.018
N_6	-0.229	-0.223	-0.353	-0.249	-0.286	-0.317	-0.339	-0.222	-0.285	-0.453	-0.266	-0.167	-0.419	-0.230
H_7	0.253	0.254	0.299	0.275	0.214	0.219	0.315	0.258	0.262	0.340	0.282	0.253	0.329	0.262
N_9	-0.328	-0.317	-0.343	-0.317	-0.317	-0.346	-0.295	-0.233	-0.234	-0.344	-0.339	-0.270	-0.352	-0.272
H_{11}	0.237	0.242	0.258	0.221	0.267	0.219	0.238	0.214	0.212	0.248	0.279	0.257	0.251	0.261

Zero point energy **ZPE**, thermal correction **TC** Kcal/mol, and entropy **S** cal/mol-K.

Table (19) : Zero Point Energy **ZPE**, Thermal Correction **TC**, Ionization Potential, net charges and dipole moments in gas phase of **24ATH**, **25ATH** and their tautomers calculated at the **MP2/6-311++G****.

	24ATH 1	**25ATH 2**	**3I4ATH 1.1**	**2A5ITH 1.2**	**5I4ATH 1.3**	**3I5ITH 1.4**	**3I5ATH 2.1**	**2A4ITH 2.2**	**3I4ITH 2.3**	**TS_1 1.1**	**TS_2 1.2**	**TS_3 1.3**	**TS_5 2.1**	**TS_6 2.2**
ZPE	55.98	56.12	55.92	56.34	56.22	56.47	55.81	56.04	56.16	52.51	52.42	52.38	52.48	51.96
TC	60.35	60.48	60.18	60.43	60.36	60.46	60.13	60.21	60.21	56.63	56.35	56.15	56.63	55.94
S	81.52	81.6	81.03	80.89	81.54	80.53	81.53	81.37	80.87	80.04	78.76	77.58	80.68	79.15
E_{HOMO} eV	-7.878	-8.038	-7.861	-9.475	-9.407	-10.014	-7.837	-9.679	-9.940					
E_{LUMO} eV	1.129	1.042	0.833	0.906	0.626	0.917	0.819	1.007	0.838					
ΔE_g eV	9.007	9.080	8.694	10.381	10.033	10.931	8.656	10.686	10.778					
IP eV	7.878	8.038	7.861	9.475	9.407	10.014	7.837	9.679	9.940					
Dipole Moment D D.M(gas)	0.601	1.055	3.661	3.825	6.074	3.206	3.831	2.564	2.730	1.857	2.902	3.417	2.578	2.161
Charge:														
N_3	-0.153	-0.110	-0.135	-0.132	-0.098	-0.054	-0.090	-0.094	-0.102	-0.150	-0.123	-0.029	-0.073	-0.073
C_4	-0.362	-0.272	-0.296	-0.139	-0.028	-0.024	-0.166	-0.602	-0.465	-0.390	-0.093	-0.279	-0.307	-0.650
C_5	-0.027	-0.215	0.041	-0.422	-0.454	-0.542	-0.271	-0.055	-0.136	-0.003	-0.525	-0.255	-0.182	-0.033
N_6	-0.301	-0.296	-0.350	-0.290	-0.284	-0.304	-0.340	-0.295	-0.266	-0.450	-0.286	-0.171	-0.437	-0.299
H_7	0.263	0.264	0.304	-0.278	0.228	0.331	0.305	0.270	0.261	0.315	0.277	0.183	0.303	0.272
N_9	-0.397	-0.373	-0.422	-0.291	-0.353	-0.320	-0.359	-0.213	-0.210	-0.407	-0.324	-0.318	-0.377	-0.254
H_{11}	0.266	0.255	0.267	0.228	0.264	0.190	0.252	0.216	0.219	0.258	0.274	0.255	0.259	0.257

Zero point energy **ZPE**, thermal correction **TC** Kcal/mol, and entropy **S** cal/mol-K.

4.2.4. ***ENERGIES AND RELATIVE STABILITIES***

The total gaseous energies (E_T), relative stabilities (ΔE), enthalpies of formation (ΔH_f), Gibbs free energies (ΔG) and energy barriers (E_a) of 2,4-diaminothiazole tautomers are depicted in Tables (20 and 21). All five structures of 2,4-diaminothiazole represent stationary point minima in their potential energy surface in both levels. The B3LYP/6-311++G** calculations of their relative stabilities show that the most stable one in gas phase is **2A5ITH** i.e. local minimum, while **3I4ATH** is the highest one in energy. The order of stability of the five structures is; **2A5ITH > 24ATH ≈ 5I4ATH > 3I5ITH > 3I4ATH.** In case of MP2 results, their stability order becomes **24ATH > 2A5ITH > 5I4ATH > 3I5ITH > 3I4ATH**.

Angelova et al. studied the tautomerism of 2,4-substituted azilidines[174] using HF and MP2/6-31+G**. The two imino forms **5I4ATH** and **2A5ITH** were detected where the latter is the most stable one by only 0.18-0.28 Kcal/mol. At MP2 / 6-31+G** the preferred one is **24ATH** but the differences in energy between **24ATH** and **5I4ATH** and **2A5ITH** are only small 0.78, 1.79 Kcal/mol, respectively.

Experimentally, NMR[38] studies showed that the imino form **2A5ITH** is the detected species of 2,4-diaminothiazole. The other structures are unlikely in DMSO because the NMR spectra show two protons bonded to C_5 atom. Therefore, B3LYP describes that equilibrium

better than MP2 method. Comparing to the results for mono-aminothiazoles (**2ATH** and **4ATH**) one can notice that, Tabls (9 and 21):

(1) The amino substitution in 4-position in case of **2ATH** destabilizes the imino form, i.e. the process **24ATH** $\rightleftharpoons$ **3I4ATH** becomes more endothermic. Consequently, the free energy change ΔG has more positive value, i.e. forbidden process. In the same time the conversion barrier ΔE^* and the activation energy E_a have the same values in both processes. The equilibrium constant K_T of (**24ATH** $\rightleftharpoons$ **3I4ATH**) is 1.61×10^7 which is higher than that for **2ATH** (1.82×10^5) i.e. the **23ITH** is more favored than **3I4ATH**.

(2) For **4ATH** tautomerization, the introduction of the substituent $-NH_2$ group in position two facilitates the hydrogen transfer **24ATH** $\rightleftharpoons$ **2A5ITH** and the reaction enthalpy becomes (-0.84 Kcal/mol) with a decrease of activation energy E_a (55.62 Kcal/mol). This is reflected as an increase of the amount of imino form since the ratio **24ATH / 2A5ITH** is 0.12 comparing to 1.82×10^5 for **4ATH / 45ITH** ratio.

(3) The existence of $-NH_2$ group in position (four) also increases the stability and the percent of the imino **5I4ATH** to reach (0.56) instead of (1.12×10^8) in case of **5ITH**.

(4) The diimino structure **3I5ITH** has only energy 2.23 Kcal/mol more than the diamino one (**24ATH**).

Table (20): Total energy in gas, water (w), and CCl_4 of **24ATH**, **25ATH** and their tautomers calculated at the **B3LYP** and **MP2/6-311++G****.

Total Energy a.u.	E_t (gas)	E_t (w)	E_t (CCl_4)
24ATH 1	-679.88601 *-678.71328*	-679.89950	-679.89172
25ATH 2	-679.87596 *-678.70513*	-679.89031	-679.88192
3I4ATH 1.1	-679.87023 *-678.69217*	-679.88552	-679.87679
2A5ITH 1.2	-679.88706 *-678.71061*	-679.90251	-679.89376
5I4ATH 1.3	-679.88607 *-678.70905*	-679.90523	-679.89415
3I5ITH 1.4	-679.88301 *-678.70548*	-679.89765	-679.88923
3I5ATH 2.1	-679.86341 *-678.68553*	-679.87879	-679.86993
2A4ITH 2.2	-679.87528 *-678.69935*	-679.88884	-679.88093
3I4ITH 2.3	-679.86567 *-678.68867*	-679.88142	-679.87217
TS_1 1.1	-679.79789 *-678.62391*	-679.80781	-679.80205
TS_2 1.2	-679.78505 *-678.60768*	-679.79738	-679.79039
TS_3 1.3	-679.73093 *-678.5612*	-679.74391	-679.73644
TS_5 2.1	-679.79041 *-678.61854*	-679.79918	-679.79412
TS_6 2.2	-679.76132 *-678.58846*	-679.77330	-679.76635

Values in italic refer to **MP2**.

Table (21): Relative stabilities conversion barrier **ΔE***(kcal/mol), activation energy $\mathbf{E_a}$ (kcal/mol), reaction enthalpy **ΔH** (kcal/mol), and the Gibbs free energy change **ΔG** (Kcal/mol), and equilibrium constant **K** of 2,4-diaminothiazole (**24ATH**) and 2,5-diaminothiazole (**25ATH**) calculated at the **B3LYP** and **MP2** levels/**6-311++G****.

	24ATH=3I4ATH	**24ATH =2A5ITH**	**24ATH =5I4ATH**	**24ATH=3I5ITH**	**25ATH =3I5ATH**	**25ATH =2A4ITH**	**25ATH =3I4ITH**
ΔE*	55.30 *56.08*	63.35 *66.26*	97.31 *95.43*		53.68 *54.34*	71.94 *73.21*	
Ea	48.17 *49.45*	55.62 *59.30*	89.94 *88.22*		45.38 *47.44*	63.70 *65.10*	
ΔE	9.90 *13.25*	-0.66 *1.68*	-0.04 *2.65*	1.88 *4.89*	7.88 *12.30*	0.43 *3.63*	6.46 *10.33*
ΔH	9.81 *13.02*	-0.84 *2.12*	-0.17 *2.90*	2.23 *5.49*	7.32 *11.64*	6.7×10^{-3} *3.28*	6.04 *10.10*
ΔG	9.83 *13.16*	-1.28 *2.30*	-0.35 *2.90*	2.08 *5.79*	7.19 *11.66*	-5.89×10^{-2} *3.35*	5.94 *10.32*
LogK	-7.2069 *-9.6475*	0.9361 *-1.6882*	2.54×10^{-1} *-2.1243*	-1.5249 *-4.2435*	-5.2720 *-8.5461*	4.32×10^{-2} *-2.4521*	-4.3505 *-7.5613*
K	1.61×10^{7} 4.44×10^{9}	0.12 *48.77*	0.56 1.33×10^{2}	33.49 1.75×10^{4}	1.87×10^{5} 3.52×10^{8}	9.05×10^{-1} 2.83×10^{2}	2.24×10^{4} 3.64×10^{7}

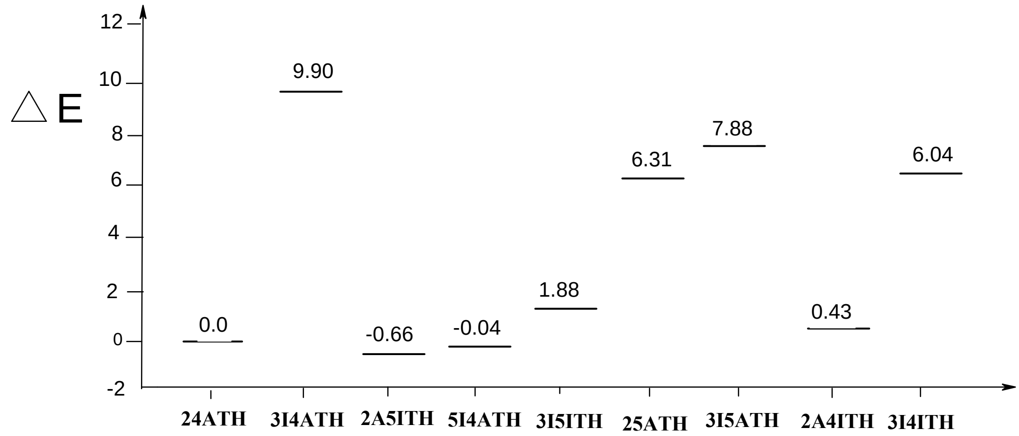
Values in italic refer to **MP2**.

Energetically, **24ATH** is less in energy than **25ATH** by 6.31 Kcal/mol whereas the value in case of the two imino forms **3I5ATH** and **3I4ATH** is only 4.28 Kcal/mol at B3LYP/6-311++G** level, Fig. (4). As in all studied cases, the amino form **25ATH** is less in energy than the three imino tautomers **3I5ATH**, **3I4ITH** and **2A4ITH** with a stability order **25ATH > 2A4ITH > 3I4ITH > 3I5ATH**. The differences in energy between these tautomers are 0.43, 6.46 and 7.88 Kcal/mol, respectively. Therefore, the stability of **25ATH** and **2A4ITH** is nearly equal, while in case of **24ATH** the imino form **2A5ITH** is the most popular one detected experimentally and theoretically. Comparing to the results of **24ATH**, one also notices that a decrease in activation energy E_a for **25ATH** case (2.79 Kcal/mol) and also a decrease in enthalpy of reaction ΔH (2.49 Kcal/mol). The Gibbs free energy change of the transformation **25ATH** $\rightleftharpoons$ **2A4ITH** is only -0.06 Kcal/mol which leads to equal amounts of the two forms (K = 9.05×10^{-1}). On the other hand, the stability of the other two imino forms **3I5ATH** and **3I4ITH** are less than **25ATH**, thus their ratios are negligible comparing to **25ATH** or **2A4ITH** tautomers (K = 1.87×10^{5} and 2.24×10^{4}), respectively. The stability order of the above tautomerization using MP2 level is

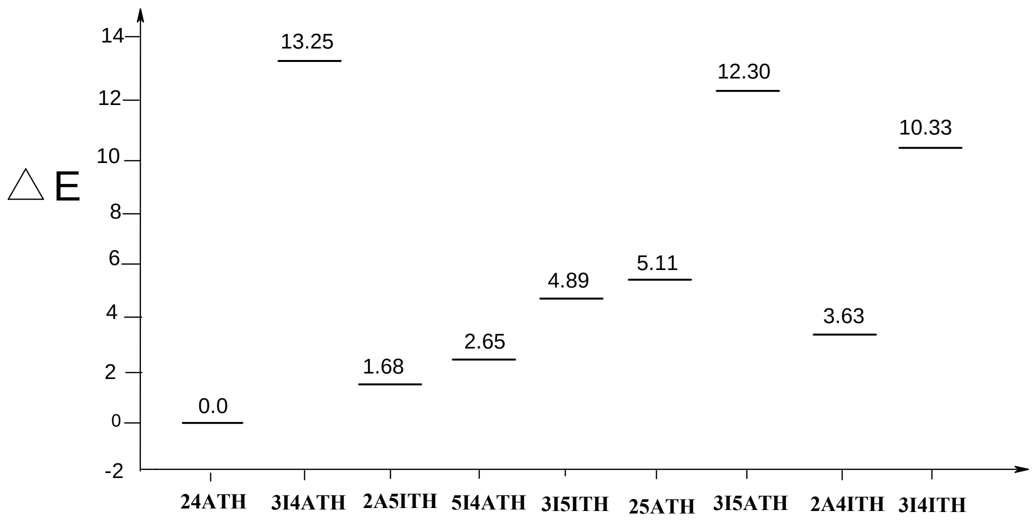
25ATH > 2A4ITH > 3I4ITH > 3I5ATH.

with equilibrium constant (K =2.83×10^{2}, 3.64×10^{7}, 3.52×10^{8}) i.e. the stability of **2A4ITH** decreases at MP2 level.

Fig (4): Relative stabilities of **24ATH** and **25ATH** tautomers calculated at the **B3LYP (A)** and **MP2 (B) / 6-311++G****.



(A)



(B)

4.2.5. ***SOLVENT EFFECT***

Tables (7,8,18 and 19) show the dipole moment of different tautomers of **2ATH**, **4ATH** and **24ATH** in gas phase, water (polar, ε = 76) and carbon tetrachloride (nonpolar, ε =36.44). The following points can be with drawn from these results:

(1) All of amino forms **2ATH**, **4ATH**, and **5ATH** and their imino tautomers are polar compounds where **5ATH** forms are more polar than **2ATH** and **4ATH** tautomers.

(2) The dipole moment of amino form is less than the corresponding imino tautomers in the three phases, except in case of **5ATH**.

(3) The dipole moment of all species increases in both solvents but in water, it has maximum value, Table (7,8,18 and 19).

(4) Therefore, it is expected that all species will be stabilized in more polar medium (water) than in less polar solvent (CCl_4).

The free energy of solvation (ΔG°_{s}) of **2ATH**, **4ATH**, **5ATH** and their imino structures with the corresponding TSs are given in Table (22). The results show that all species are more stabilized with different extents in both media but the stabilization energy in water is greater. The relative free energy in the two solvents, ΔG°_{soln}, and the equilibrium constants are given in the same table. The relative free energies (ΔG°_{soln}) in the two solutions are less positive than in gas phase ΔG°_{g}, meaning that the imino

Table (22): The solvation energy G°_{s}, the free energy of solvation ΔG°_{s}, the relative free energy in the solvents ΔG°_{soln}, the relative free energy in gas phase ΔG°_{g}, the equilibrium constants K_{soln} in water (w) and CCl_4 and the equilibrium constants K_g in gas phase of **2ATH**, **4ATH**, **5ATH** and their tautomers calculated at the **B3LYP/6-311++G****.

Tautomers	G°_{s} Kcal/mol	ΔG°_{s} Kcal/mol	ΔG°_{g} Kcal/mol	ΔG°_{soln} Kcal/mol	K_{soln}	K_g
2ATH						
(w)	-6.38	0.0				
(CCl_4)	-2.72	0.0				
23ITH						
(w)	-7.14	-0.76	7.18	6.42	5.08×10^{4}	1.82×10^{5}
(CCl_4)	-3.05	-0.33		6.85	1.05×10^{5}	
25ITH						
(w)	-7.76	-1.38	10.98	9.60	1.09×10^{7}	1.12×10^{8}
(CCl_4)	-3.23	-0.51		10.47	4.72×10^{7}	
4ATH						
(w)	-5.06	0.0				
(CCl_4)	-2.45	0.0				
45ITH						
(w)	-6.23	-1.17	7.17	6.00	2.50×10^{4}	1.82×10^{5}
(CCl_4)	-2.69	-0.24		6.93	1.2×10^{5}	
5ATH						
(w)	-7.12	0.0				
(CCl_4)	-2.97	0.0				
54ITH						
(w)	-6.04	1.08	5.40	6.48	5.62×10^{4}	9.07×10^{3}
(CCl_4)	-2.57	0.40		5.80	1.78×10^{4}	

amount increases relative to its amino form, the reverse is found in case of **5ATH**. For aminothiazoles, one notices that in spite of the solvent stability of imino form is greater than its amino, the latter still the predominant species in solution and thus the same stability trends of the tautomers as in the case of the gaseous phase are found:

2ATH > 23ITH > 25ITH

4ATH > 45ITH

5ATH > 54ITH

The solvation energy of **24ATH** tautomers given in Table (23) shows that all the species have been stabilized in the two solvents more than in gas phase as in case of mono thiazole. The stabilization in water is more pronounced due to high values of their dipole moment. **24ATH** is the least stabilized one (0.792 D) while **5I4ATH** is the most stabilized form (9.182 D, 7.683 D) in both solutions. Therefore, the imino tautomer **5I4ATH** will be more predominant than **2A5ITH** in both solvents. The order of stability of **24ATH** tautomers changed in both solutions to be:

5I4ATH > 2A5ITH > 24ATH > 3I5ITH > 3I4ATH.

In case of **25ATH**, the relative free energy change in solution show that the order of amounts of **25ATH** tautomers becomes

25ATH > 2A4ITH > 3I4ITH > 3I5ATH.

i.e. the relative stability of **25ATH** and **2A4ITH** exchanged from gas phase to solutions.

Table (23): The solvation energy G_s°, the free energy of solvation ΔG_s°, the relative free energy in the solvents ΔG_{soln}°, the relative free energy in gas phase ΔG_g°, the equilibrium constants K_{soln} in water (w) and CCl_4 and the equilibrium constants K_g in gas phase of **24ATH**, **25ATH** and their tautomers calculated at the **B3LYP/6-311++G****.

Tautomers	G°_s Kcal/mol	ΔG°_s Kcal/mol	ΔG°_g Kcal/mol	ΔG°_{soln} Kcal/mol	K_{soln}	K_g
24ATH						
(w)	-8.46	0.0				
(CCl_4)	-3.58	0.0				
3I4ATH						
(w)	-9.59	-1.13	9.83	8.70	2.38×10^{6}	1.61×10^{7}
(CCl_4)	-4.12	-0.54		9.29	6.44×10^{6}	
2A5ITH						
(w)	-9.69	-1.23	-1.28	-2.51	1.54×10^{-2}	0.12
(CCl_4)	-4.20	-0.62		-1.90	4.05×10^{-2}	
5I4ATH						
(w)	-12.02	-3.56	-0.35	-3.91	1.36×10^{-3}	0.56
(CCl_4)	-5.07	-1.49		-1.84	4.48×10^{-2}	
3I5ITH						
(w)	-9.19	-0.73	2.08	1.35	9.76	33.49
(CCl_4)	-3.90	-0.32		1.76	19.50	
25ATH						
(w)	-9.00	0.0				
(CCl_4)	-3.74	0.0				
3I5ATH						
(w)	-9.65	-0.65	7.19	6.54	6.22×10^{4}	1.87×10^{5}
(CCl_4)	-4.09	-0.35		6.84	1.03×10^{5}	
2A4ITH						
(w)	-8.51	0.49	-5.89×10^{-2}	0.43	2.07	9.05×10^{-1}
(CCl_4)	-3.55	0.19		0.13	1.25	
3I4ITH						
(w)	-9.88	-0.88	5.94	5.06	5.11×10^{3}	2.24×10^{4}
(CCl_4)	-4.08	-0.34		5.60	1.27×10^{4}	

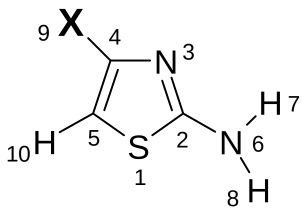
4.3. SUBSTITUENT EFFECT

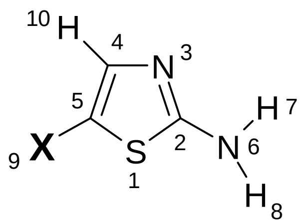
4.3.1. 4- OR 5-SUBSTITUTED 2-AMINOTHIAZOLE

The reactivity of 4- or 5-substituted 2-aminothiazoles towards nucleophilic reagents has been known to be related to the presence of tautomeric forms of these compounds(175). The sensitivity of five-membered heterocycles to the electronic effects of substituents is higher than that observed for six-membered heterocycles or homocycles. The basicity of the aza nitrogen in 2-aminothiazole derivatives is strongly affected by the substituent electronic effect.

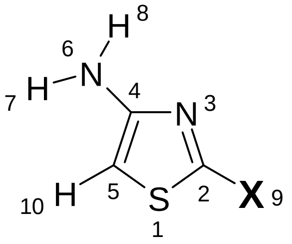
Spectroscopic investigations on different 2-aminothiazole derivatives reveal that the amino aromatic form is the more populated form, but strong electron withdrawing substituents bonded to the amino group shift the equilibrium towards the imino form(175). Another parameter that affects the position of this equilibrium is the polarity of the medium (solvent). HMO calculations supported these findings(175). In this part, high level of calculations at B3LYP/6-311++G** will be applied for various substituted 2- and 4-aminothiazoles to quantitatively devote the effect of its type and position on their equilibrium and energetics.

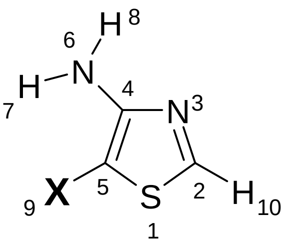
Fig (5): Structure and numbering system of 4- and 5-substituted-2-amino-thiazole, 2- and 5-substituted-4-aminothiazole, and 2-(N-nitro-amino)thiazole.



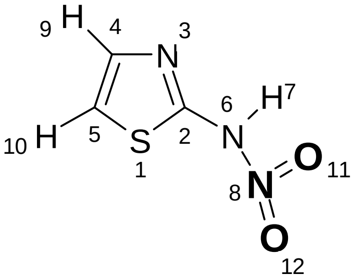


X=F, Cl, CHO, CH_3 and NO_2





X=F and CH_3



4.3.1.1. ***GEOMETRY:***

In this part, all calculations were done using B3LYP/6-311++G** and MP2/6-311++G** methods. The structural parameters of the optimized form of each derivative are given in Tables (24 and 25). The data depicted in these tables show that:

Comparing to the geometry of **2ATH** and **23ITH**:

(1) Methyl group (electron donating) in position four increases only the bond length (C_4-N_3) in both forms. The negative charge on endocyclic nitrogen and C_5 atom decreases leading to a decrease in its dipole moment, while the dipole moment of the imino form increases.

(2) Electron accepting (withdrawing) groups (F, Cl) shortens the C_4-N_3 bond length in the two forms. The substituents NO_2 and CHO disturb the geometry of thiazole cycle due to their participating in ring delocalization and certain interactions between the negatively charge carbonyl or nitro oxygen with hydrogen C_5, C_5H (O...H=2.62 Å). Both substituents increase the dipole moment of amino and imino forms and the corresponding TSs.

(3) The substituent effect in position five on **2ATH** and **23ITH** geometry is more pronounced than that in position four in case of electron withdrawing ones while 5-CH_3 group elongates only S-C_5 bond.

(4) The delocalization of exocyclic nitrogen atom lone pair decreases upon 5-CHO and 5-NO_2 substitution leading to more double and single bond character of C_2N_6 and C_2N_3 bonds, respectively.

Table (24): Geometrical parameters of **2ATH**, and **4-substituted(F, Cl, CH_3, CHO, and NO_2)-2ATH** calculated at **B3LYP** and **MP2 / 6-311++G****.

Bond Length Å	2ATH (1)	4-F (2)	4-Cl (3)	4-CH_3 (4)	4-CHO (5)	4-NO_2 (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	TS (2)	TS (3)	TS (4)	TS (5)	TS (6)
S_1C_2	1.767	1.765	1.765	1.765	1.776	1.778	1.809	1.810	1.810	1.806	1.822	1.832	1.747	1.747	1.743	1.754	1.759
	1.739	*1.737*	*1.738*	*1.738*	*1.744*	*1.744*	*1.780*	*1.781*	*1.782*	*1.779*	*1.788*	*1.794*	*1.729*	*1.729*	*1.727*	*1.735*	*1.737*
S_1C_5	1.749	1.752	1.750	1.751	1.733	1.735	1.768	1.775	1.770	1.769	1.744	1.744	1.781	1.780	1.780	1.761	1.762
	1.722	*1.725*	*1.722*	*1.723*	*1.711*	*1.715*	*1.747*	*1.755*	*1.749*	*1.749*	*1.731*	*1.734*	*1.750*	*1.747*	*1.748*	*1.734*	*1.738*
C_2N_3	1.298	1.302	1.301	1.297	1.295	1.298	1.385	1.388	1.387	1.384	1.382	1.384	1.350	1.348	1.344	1.342	1.346
	1.310	*1.312*	*1.311*	*1.308*	*1.309*	*1.312*	*1.383*	*1.389*	*1.388*	*1.384*	*1.385*	*1.389*	*1.352*	*1.350*	*1.346*	*1.348*	*1.353*
N_3C_4	1.379	1.359	1.368	1.386	1.384	1.363	1.385	1.376	1.383	1.391	1.393	1.377	1.360	1.367	1.379	1.380	1.363
	1.376	*1.358*	*1.368*	*1.382*	*1.378*	*1.358*	*1.381*	*1.376*	*1.383*	*1.389*	*1.388*	*1.372*	*1.363*	*1.371*	*1.381*	*1.379*	*1.363*
C_4C_5	1.356	1.353	1.355	1.359	1.365	1.358	1.341	1.334	1.338	1.344	1.352	1.345	1.352	1.354	1.359	1.363	1.357
	1.370	*1.364*	*1.369*	*1.371*	*1.378*	*1.371*	*1.352*	*1.342*	*1.349*	*1.353*	*1.361*	*1.353*	*1.361*	*1.367*	*1.369*	*1.376*	*1.369*
C_4X_9	1.082	1.338	1.742	1.498	1.476	1.467	1.080	1.334	1.732	1.495	1.469	1.442	1.331	1.733	1.495	1.476	1.458
	1.083	*1.334*	*1.720*	*1.495*	*1.475*	*1.461*	*1.081*	*1.330*	*1.711*	*1.492*	*1.470*	*1.444*	*1.328*	*1.712*	*1.493*	*1.474*	*1.452*
C_2N_6	1.377	1.370	1.372	1.377	1.373	1.367	1.272	1.269	1.269	1.273	1.268	1.264	1.315	1.316	1.322	1.317	1.312
	1.389	*1.384*	*1.385*	*1.390*	*1.385*	*1.379*	*1.285*	*1.281*	*1.282*	*1.285*	*1.281*	*1.278*	*1.329*	*1.331*	*1.336*	*1.331*	*1.326*
N_6H_7	1.011	1.010	1.010	1.011	1.011	1.010	2.571	2.600	2.589	2.567	2.579	2.632	1.418	1.416	1.408	1.418	1.419
	1.013	*1.013*	*1.013*	*1.013*	*1.013*	*1.013*	*2.562*	*2.581*	*2.568*	*2.555*	*2.556*	*2.603*	*1.434*	*1.433*	*1.430*	*1.437*	*1.432*
$O\text{-}H_{10}$					2.859	2.607					2.838	2.671				2.869	2.647
					2.851	*2.630*					*2.836*	*2.685*				*2.858*	*2.653*

Values in italic refer to **MP2**.

Table (24): Continue.

Bond Angle degree	**2ATH (1)**	**4-F (2)**	**4-Cl (3)**	**4-CH_3 (4)**	**4-CHO (5)**	**4-NO_2 (6)**	**23ITH (1)**	**Imino (2)**	**Imino (3)**	**Imino (4)**	**Imino (5)**	**Imino (6)**	**TS (2)**	**TS (3)**	**TS (4)**	**TS (5)**	**TS (6)**
$N_3C_2S_1$	114.8	114.9	114.9	114.8	114.4	114.6	106.4	106.7	106.6	106.5	106.1	106.2	112.5	112.4	112.3	112.0	112.3
	115.3	*115.5*	*115.5*	*115.3*	*115.1*	*115.4*	*107.0*	*107.5*	*107.3*	*107.1*	*106.9*	*107.1*	*112.8*	*112.6*	*112.3*	*112.2*	*112.6*
$C_4N_3C_2$	110.8	109.6	110.0	111.4	111.0	109.8	117.0	115.5	116.1	117.6	117.1	115.6	112.5	113.1	114.6	113.9	112.5
	109.9	*108.8*	*109.3*	*110.6*	*109.9*	*108.6*	*116.6*	*114.5*	*115.2*	*116.8*	*116.1*	*114.5*	*111.8*	*112.6*	*114.1*	*113.3*	*111.6*
$C_5C_4X_9$	116.7	123.7	123.6	115.4	116.2	122.0	114.2	116.8	126.8	128.0	113.3	116.1	125.2	115.3	112.8	113.6	123.6
	116.0	*123.9*	*124.0*	*114.9*	*115.9*	*122.4*	*113.3*	*116.0*	*127.4*	*128.4*	*112.8*	*115.7*	*125.7*	*113.9*	*111.8*	*112.6*	*124.2*
$N_6C_2S_1$	121.1	121.4	121.3	121.1	120.9	121.1	130.4	130.4	130.4	130.4	130.0	129.7	141.5	141.4	141.2	141.0	141.2
	121.1	*121.3*	*121.3*	*121.1*	*121.0*	*121.2*	*130.6*	*130.5*	*130.6*	*130.6*	*130.5*	*130.3*	*140.0*	*140.1*	*140.1*	*139.9*	*140.1*
$H_7N_6C_2$	113.4	114.5	114.2	113.5	114.0	114.8	118.7	120.7	120.0	118.5	118.7	121.8	77.1	77.0	76.5	74.2	76.9
	110.6	*111.4*	*111.1*	*110.6*	*111.1*	*111.8*	*118.7*	*119.4*	*118.5*	*117.7*	*117.4*	*120.3*	*77.0*	*76.9*	*76.6*	*72.5*	*76.8*
$X_9C_4N_3$	118.8	117.2	118.4	118.7	119.1	119.4	119.1	115.9	117.8	119.2	125.9	118.6	118.3	119.6	120.4	125.5	120.3
	119.2	*117.6*	*118.8*	*119.0*	*119.3*	*119.2*	*119.7*	*116.2*	*118.2*	*119.4*	*126.1*	*118.4*	*118.7*	*120.0*	*120.7*	*125.7*	*120.1*

Values in italic refer to **MP2**.

Table (24): Continue.

Dihedral Angle degree	2ATH (1)	4-F (2)	4-Cl (3)	4-CH_3 (4)	4-CHO (5)	4-NO_2 (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	TS (2)	TS (3)	TS (4)	TS (5)	TS (6)
$N_3C_2S_1N_6$	176.4	176.6	176.6	176.4	176.3	-176.6	180.0	180.0	180.0	180.0	180.0	180.0	-177.4	175.5	174.7	-174.4	-176.0
	180.0	*174.1*	*173.9*	*174.1*	*173.9*	*-174.3*	*180.0*	*179.8*	*179.5*	*180.0*	*179.7*	*179.4*	*-166.4*	*166.2*	*166.7*	*-166.2*	*-166.8*
$C_4N_3C_2N_6$	0.1	176.6	176.6	176.5	176.3	-176.6	0.0	179.8	179.9	179.9	180.0	180.0	-176.7	-2.9	173.2	-172.5	-174.0
	0.7	*174.7*	*174.5*	*174.6*	*174.3*	*-175.0*	*0.1*	*-172.6*	*-171.9*	*173.0*	*-171.9*	*-172.1*	*-163.4*	*-8.1*	*164.0*	*-162.4*	*-162.2*
$C_5C_4X_9N_3$	0.4	179.4	179.4	0.4	0.4	-179.4	0.0	0.2	180.0	180.0	0.0	0.0	-179.0	2.7	3.1	-3.5	-178.2
	0.2	*179.0*	*178.7*	*0.3*	*0.6*	*-179.1*	*0.0*	*-6.2*	*-177.3*	*177.6*	*-7.0*	*-7.2*	*-174.5*	*7.6*	*6.8*	*-8.1*	*-172.3*
$N_6C_2S_1N_3$	176.4	176.6	176.6	176.4	176.3	-176.6	180.0	180.0	180.0	180.0	180.0	180.0	-177.4	175.5	174.7	-174.4	-176.0
	180.0	*174.1*	*173.9*	*174.1*	*173.9*	*-174.3*	*180.0*	*179.8*	*179.5*	*180.0*	*179.7*	*179.4*	*-166.4*	*166.2*	*166.7*	*-166.2*	*-166.8*
$H_7N_6C_2N_3$	15.4	15.3	14.8	15.8	14.8	-13.5	0.0	0.4	0.4	0.2	0.1	0.0	0.5	-178.1	1.8	-1.3	0.7
	16.2	*17.4*	*16.4*	*16.8*	*16.2*	*-15.6*	*0.1*	*-12.6*	*-12.6*	*9.9*	*-11.3*	*-11.5*	*2.0*	*-173.0*	*-3.0*	*-2.2*	*1.7*
$X_9C_4N_3C_2$	179.9	179.8	179.8	180.0	179.8	179.8	180.0	179.9	179.9	179.9	180.0	180.0	179.4	-178.8	-178.4	177.8	178.8
	179.2	*179.3*	*179.1*	*179.2*	*178.3*	*179.5*	*180.0*	*175.7*	*175.4*	*-176.0*	*176.1*	*174.9*	*177.8*	*-177.5*	*-177.7*	*172.8*	*178.2*

Values in italic refer to **MP2**.

Table (25): Geometrical parameters of **2ATH**, and **5-substituted(F, Cl, CH_3, CHO, and NO_2)-2ATH** calculated at the **B3LYP** and **MP2/6-311++G****.

Bond Length Å	**2ATH (1)**	**5-F (2)**	**5-Cl (3)**	**5-CH_3 (4)**	**5-CHO (5)**	**5-NO_2 (6)**	**23ITH (1)**	**Imino (2)**	**Imino (3)**	**Imino (4)**	**Imino (5)**	**Imino (6)**	**TS (2)**	**TS (3)**	**TS (4)**	**TS (5)**	**TS (6)**
S_1C_2	1.767	1.776	1.770	1.769	1.757	1.762	1.809	1.823	1.816	1.809	1.803	1.809	1.754	1.749	1.746	1.736	1.743
	1.739	*1.748*	*1.743*	*1.742*	*1.734*	*1.739*	*1.780*	*1.791*	*1.786*	*1.781*	*1.778*	*1.785*	*1.737*	*1.732*	*1.730*	*1.722*	*1.728*
S_1C_5	1.749	1.758	1.759	1.765	1.768	1.754	1.768	1.767	1.773	1.783	1.785	1.767	1.782	1.787	1.796	1.803	1.784
	1.722	*1.732*	*1.731*	*1.734*	*1.733*	*1.724*	*1.747*	*1.750*	*1.753*	*1.759*	*1.759*	*1.746*	*1.753*	*1.755*	*1.759*	*1.763*	*1.753*
C_2N_3	1.298	1.294	1.297	1.295	1.312	1.316	1.385	1.380	1.384	1.381	1.397	1.401	1.340	1.344	1.341	1.361	1.366
	1.310	*1.306*	*1.308*	*1.308*	*1.316*	*1.316*	*1.383*	*1.383*	*1.384*	*1.382*	*1.392*	*1.394*	*1.343*	*1.346*	*1.345*	*1.358*	*1.359*
N_3C_4	1.379	1.384	1.378	1.381	1.359	1.357	1.385	1.394	1.387	1.389	1.362	1.360	1.384	1.375	1.377	1.347	1.346
	1.376	*1.381*	*1.376*	*1.378*	*1.364*	*1.367*	*1.381*	*1.395*	*1.387*	*1.387*	*1.365*	*1.366*	*1.384*	*1.378*	*1.378*	*1.357*	*1.359*
C_4C_5	1.356	1.348	1.355	1.358	1.373	1.367	1.341	1.334	1.340	1.342	1.357	1.352	1.347	1.354	1.356	1.375	1.371
	1.370	*1.361*	*1.369*	*1.371*	*1.379*	*1.369*	*1.352*	*1.344*	*1.350*	*1.352*	*1.361*	*1.354*	*1.360*	*1.366*	*1.369*	*1.378*	*1.369*
C_5X	1.078	1.337	1.730	1.495	1.455	1.423	1.077	1.337	1.728	1.493	1.457	1.424	1.338	1.730	1.494	1.449	1.413
	1.080	*1.333*	*1.712*	*1.495*	*1.466*	*1.440*	*1.079*	*1.333*	*1.710*	*1.492*	*1.463*	*1.433*	*1.334*	*1.713*	*1.494*	*1.462*	*1.432*
C_2N_6	1.377	1.379	1.375	1.379	1.361	1.355	1.272	1.269	1.270	1.273	1.268	1.265	1.322	1.319	1.323	1.310	1.307
	1.389	*1.391*	*1.389*	*1.391*	*1.380*	*1.377*	*1.285*	*1.282*	*1.282*	*1.285*	*1.281*	*1.279*	*1.335*	*1.334*	*1.337*	*1.325*	*1.321*
N_6H_7	1.011	1.012	1.011	1.011	1.009	1.009	2.571	2.574	2.573	2.574	2.559	2.558	1.423	1.416	1.413	1.400	1.403
	1.013	*1.014*	*1.014*	*1.014*	*1.013*	*1.013*	*2.562*	*2.547*	*2.554*	*2.557*	*2.555*	*2.555*	*1.439*	*1.434*	*1.433*	*1.414*	*1.411*
$O\text{-}H_{10}$					2.861	2.685					2.806	2.635				2.860	2.691
					2.845	*2.687*					*2.793*	*2.650*				*2.837*	*2.686*

Values in italic refer to **MP2**.

Table (25): Continue.

Bond Angle degree	2ATH (1)	5-F (2)	5-Cl (3)	5-CH_3 (4)	5-CHO (5)	5-NO_2 (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	TS (2)	TS (3)	TS (4)	TS (5)	TS (6)
$N_3C_2S_1$	114.8 *115.3*	115.3 *115.9*	115.0 *115.5*	114.7 *115.2*	115.3 *115.6*	115.9 *116.3*	106.4 *107.0*	107.0 *107.9*	106.7 *107.4*	106.3 *107.0*	106.7 *107.2*	107.4 *107.9*	112.8 *113.0*	112.5 *112.6*	112.1 *112.2*	112.6 *112.6*	113.1 *113.4*
$C_4N_3C_2$	110.8 *109.9*	111.6 *110.7*	111.4 *110.5*	110.7 *109.8*	110.7 *109.9*	110.7 *110.0*	117.0 *116.6*	117.4 *116.1*	117.3 *116.3*	116.9 *116.0*	117.1 *116.6*	117.0 *116.5*	114.5 *114.0*	114.4 *113.9*	113.9 *113.4*	114.2 *113.7*	114.2 *113.6*
$C_5C_4N_3$	116.7 *116.0*	114.6 *114.2*	115.7 *115.3*	117.6 *117.0*	117.3 *116.4*	115.7 *114.7*	(114.2) *113.3*	112.3 *111.7*	113.4 *112.8*	115.1 *114.2*	114.7 *114.7*	113.0 *112.1*	112.0 *111.0*	113.2 *112.2*	115.0 *113.8*	114.7 *113.5*	112.8 *111.9*
$N_6C_2S_1$	121.1 *121.1*	120.1 *120.0*	120.8 *120.6*	121.0 *120.9*	121.8 *121.5*	121.5 *121.0*	130.4 *130.6*	129.4 *129.6*	130.0 *130.2*	130.3 *130.5*	131.2 *131.2*	130.9 *107.9*	139.6 *138.5*	140.7 *139.4*	140.9 *139.8*	142.1 *141.2*	141.8 *140.7*
$H_7N_6C_2$	113.4 *110.6*	112.7 *110.0*	113.4 *110.4*	113.1 *110.4*	115.6 *111.6*	116.6 *112.0*	118.7 *118.7*	118.8 *116.8*	118.8 *117.6*	118.9 *117.8*	118.5 *118.5*	118.7 *118.7*	76.6 *76.7*	76.7 *76.7*	76.5 *76.6*	76.7 *76.5*	76.9 *76.7*
$X_9C_5C_4$	129.4 *128.6*	128.3 *127.7*	128.3 *127.5*	129.5 *128.4*	128.5 *127.5*	127.6 *126.9*	127.7 *127.1*	126.9 *126.7*	126.9 *126.6*	128.9 *128.1*	126.0 *125.2*	125.1 *124.9*	128.1 *127.0*	128.0 *126.9*	129.7 *128.0*	127.9 *126.5*	127.2 *126.1*

Values in italic refer to **MP2**.

Table (25): continue.

Dihedral Angle degree	2ATH (1)	5-F (2)	5-Cl (3)	5-CH_3 (4)	5-CHO (5)	5-NO_2 (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	Ts (2)	Ts (3)	Ts (4)	Ts (5)	Ts (6)
$N_3C_2S_1N_6$	176.4	175.7	176.1	176.2	177.4	177.9	180.0	180.0	180.0	180.0	180.0	180.0	170.5	172.9	172.9	-180.0	180.0
	180.0	*173.3*	*173.5*	*173.8*	*174.0*	*174.2*	*180.0*	*179.6*	*179.5*	*180.0*	*179.6*	*-179.8*	*164.2*	*165.3*	*165.3*	*-169.8*	*-170.5*
$C_4N_3C_2N_6$	0.1	175.7	176.2	176.2	177.5	178.0	0.0	179.7	180.0	179.9	180.0	180.0	168.2	171.2	171.1	180.0	180.0
	0.7	*174.0*	*174.2*	*174.4*	*174.7*	*174.7*	*0.1*	*-170.7*	*-172.3*	*172.9*	*-177.1*	*177.1*	*161.1*	*162.5*	*162.9*	*-168.2*	*-168.2*
$C_5C_4N_3C_2$	0.4	0.4	0.4	0.5	0.2	0.1	0.0	0.3	0.0	0.1	0.0	-0.0	4.5	3.6	4.0	0.0	0.0
	0.2	*0.1*	*0.0*	*0.1*	*0.4*	*0.5*	*0.0*	*-7.5*	*-6.4*	*5.9*	*-2.6*	*2.1*	*6.8*	*6.7*	*6.8*	*-4.5*	*-3.9*
$N_6C_2S_1N_3$	176.4	175.7	176.1	176.2	177.4	177.9	180.0	180.0	180.0	180.0	180.0	180.0	170.5	172.9	172.9	180.0	180.0
	180.0	*173.3*	*173.5*	*173.8*	*174.0*	*174.2*	*180.0*	*179.6*	*179.5*	*180.0*	*179.6*	*-179.8*	*164.2*	*165.3*	*165.3*	*-169.8*	*-170.5*
$H_7N_6C_2N_3$	15.4	13.0	14.1	15.0	13.0	10.4	0.0	0.6	0.1	0.1	0.0	0.0	-1.8	-1.6	-1.9	0.0	-0.0
	16.2	*11.7*	*13.7*	*15.3*	*17.8*	*17.0*	*0.1*	*-14.3*	*-11.3*	*10.6*	*-3.7*	*3.2*	*-2.4*	*-2.6*	*-2.9*	*2.9*	*2.3*
$X_9C_5C_4N_3$	179.0	178.5	178.8	179.0	179.3	179.4	180.0	179.9	180.0	180.0	180.0	180.0	174.8	175.9	176.3	-180.0	180.0
	177.9	*177.7*	*177.3*	*177.6*	*176.0*	*176.7*	*180.0*	*-176.2*	*-177.1*	*177.0*	*179.8*	*178.5*	*172.0*	*171.9*	*171.8*	*-171.5*	*-171.8*

Values in italic refer to **MP2**.

(5) The endocyclic nitrogen atom charge is more influenced by 4-substituents than by 5-substitution.

(6) The charges at C_5 and H_7 becomes more positive comparing to their corresponding charges at the parent **2ATH**, therefore the nucleophilicity of C_5 increases upon substitution and also the acidity of H_7.

(7) The substituent at position five does not affect the acidity of H_7, while increases only the positive charge at C_4 in case of X = F, NO_2 and CHO.

4.3.1.2. ***IONIZATION POTENTIAL***

The influence of the studied substituents on the other ground state properties of **2ATH** and its tautomer **23ITH** is collected in Tables (26 and 27) indicating the following:

(1) The $–CH_3$ group in 4-position destabilizes the HOMO of **2ATH** and **23ITH** but not affect the energy of their LUMO, at the MP2 method. (2) The other substituents in position four (electron withdrawing) stabilize the two MOs HOMO and LUMO of the two tautomers. Therefore, the IP of these molecules is higher than in case of unsubstituted tautomers and $–CH_3$ derivative.

The order of IP of 4-substituted series is

$4NO_2$ > 4CHO > 4Cl > 4F > 4H > $4CH_3$ (B3LYP),

$4NO_2$ > 4CHO > 4F > 4Cl > 4H > $4CH_3$ (MP2).

Table (26): Dipole moment in gas, water (w), and CCl_4, entropy **S**, zero point energy **ZPE**, Thermal correction **TC**, energy gap **ΔE_g**, **E_{HOMO}** and **E_{LUMO}** and Mülliken charges of **2ATH**, and **4-substituted-2ATH** calculated at the **B3LYP** and **MP2 / 6-311++G****.

Parameters	2ATH (1)	4-F (2)	4-Cl (3)	4-CH_3 (4)	4-CHO (5)	4-NO_2 (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	TS (2)	TS (3)	TS (4)	TS (5)	TS (6)
ZPE	45.02	39.90	38.94	62.23	50.53	46.41	44.76	39.63	38.68	62.07	50.39	46.11	36.01	35.05	58.49	46.78	42.53
Kcal/mol	*45.37*	*40.26*	*39.33*	*62.79*	*50.84*	*46.65*	*44.43*	*39.86*	*38.99*	*62.61*	*52.75*	*46.39*	*36.80*	*35.79*	*59.35*	*47.22*	*43.16*
TC	48.42	43.83	43.10	66.66	55.24	51.38	48.15	43.58	42.86	66.51	55.08	51.05	39.97	39.18	62.85	51.4	47.50
Kcal/mol	*48.77*	*44.20*	*43.45*	*67.30*	*55.56*	*51.74*	*47.58*	*43.81*	*43.15*	*67.06*	*57.00*	*51.41*	*40.48*	*39.70*	*63.59*	*51.74*	*48.00*
S	74.30	78.93	81.78	82.00	85.43	89.02	74.49	79.61	82.40	82.75	85.75	88.53	80.55	82.24	81.94	85.46	89.61
Cal mol^{-1}	*74.44*	*79.15*	*81.53*	*82.69*	*85.72*	*90.52*	*72.81*	*79.51*	*82.15*	*82.52*	*83.15*	*89.40*	*77.72*	*80.46*	*81.07*	*84.72*	*88.76*
E_{HOMO}	-6.074	-6.199	-6.221	-5.886	-6.542	-6.931	-5.704	-5.946	-5.943	-5.551	-6.221	-6.667					
Kcal/mol	*-8.536*	*-8.778*	*-8.689*	*-8.313*	*-8.923*	*-9.508*	*-8.085*	*-8.430*	*-8.373*	*-7.940*	*-8.539*	*-9.108*					
E_{LUMO}	-0.629	-0.844	-0.912	-0.520	-2.090	-2.743	-0.411	-0.737	-0.800	-0.547	-2.525	-3.361					
Kcal/mol	*1.113*	*0.974*	*0.991*	*1.110*	*0.912*	*0.767*	*0.901*	*1.124*	*1.124*	*0.884*	*1.018*	*0.288*					
ΔE_g eV	5.445	5.355	5.309	5.366	4.452	4.188	5.293	5.209	5.143	5.004	3.696	3.306					
	9.649	*9.752*	*9.680*	*9.423*	*9.835*	*10.275*	*8.986*	*9.554*	*9.497*	*8.824*	*9.557*	*9.396*					
IP eV	6.074	6.199	6.221	5.886	6.542	6.931	5.704	5.946	5.943	5.551	6.221	6.667					
	8.536	*8.778*	*8.689*	*8.313*	*8.923*	*9.508*	*8.085*	*8.430*	*8.373*	*7.940*	*8.539*	*9.108*					
Dipole Moment D																	
D.M (gas)	1.705	3.543	3.416	1.327	4.962	6.722	2.728	1.359	1.608	3.232	0.925	3.494	1.913	1.750	1.230	2.928	5.080
	1.762	*3.324*	*3.093*	*1.435*	*4.280*	*5.983*	*2.807*	*1.553*	*1.826*	*3.216*	*0.480*	*2.918*	*1.989*	*1.826*	*1.856*	*2.361*	*4.454*
D.M (W)	2.293	4.722	4.643	1.735	6.533	9.072	3.678	1.846	2.122	4.318	1.170	4.831	2.510	2.398	1.628	3.849	6.884
D.M(CCL_4)	1.928	4.029	3.926	1.467	5.637	7.692	3.143	1.567	1.826	3.722	1.021	4.026	2.152	2.007	1.398	3.321	5.813

Values in italic refer to **MP2**.

Table (26): Continue.

Charge	2ATH (1)	4-F (2)	4-Cl (3)	$4\text{-}CH_3$ (4)	4-CHO (5)	$4\text{-}NO_2$ (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	TS (2)	TS (3)	TS (4)	TS (5)	TS (6)
N_3	-0.146	-0.194	-0.060	-0.069	-0.076	-0.126	-0.069	-0.144	-0.023	0.019	-0.020	-0.087	-0.237	-0.066	-0.064	-0.095	-0.186
	-0.116	*-0.160*	*-0.039*	*-0.037*	*-0.050*	*-0.084*	*-0.109*	*-0.156*	*-0.033*	*-0.015*	*-0.056*	*-0.102*	*-0.164*	*-0.027*	*-0.018*	*-0.057*	*-0.130*
C_4	-0.295	-0.168	-0.554	-0.398	-0.401	-0.564	-0.204	-0.075	-0.388	-0.350	-0.163	-0.535	-0.171	-0.643	-0.508	-0.409	-0.625
	-0.283	*-0.123*	*-0.439*	*-0.297*	*-0.300*	*-0.472*	*-0.187*	*-0.052*	*-0.313*	*-0.224*	*-0.067*	*-0.462*	*-0.129*	*-0.472*	*-0.340*	*-0.254*	*-0.504*
C_5	-0.143	0.064	-0.069	0.294	0.340	0.288	-0.217	0.025	-0.125	0.427	0.514	0.484	0.030	-0.047	0.391	0.450	0.363
	-0.211	*-0.012*	*-0.149*	*-0.912*	*0.202*	*0.151*	*-0.261*	*-0.007*	*-0.174*	*0.243*	*0.294*	*0.350*	*-0.009*	*-0.128*	*0.215*	*0.247*	*0.237*
N_6	-0.214	-0.232	-0.214	-0.230	-0.234	-0.223	-0.342	-0.337	-0.343	-0.373	-0.361	-0.324	-0.463	-0.453	-0.453	-0.449	-0.436
	-0.285	*-0.302*	*-0.285*	*-0.304*	*-0.307*	*-0.295*	*-0.353*	*-0.338*	*-0.339*	*-0.368*	*-0.355*	*-0.323*	*-0.442*	*-0.442*	*-0.458*	*-0.444*	*-0.419*
H_7	0.257	0.262	0.261	0.255	0.262	0.270	0.317	0.338	0.329	0.309	0.317	0.338	0.363	0.357	0.331	0.339	0.382
	0.266	*0.270*	*0.269*	*0.164*	*0.270*	*0.277*	*0.333*	*0.330*	*0.316*	*0.308*	*0.308*	*0.328*	*0.328*	*0.325*	*0.310*	*0.314*	*0.349*

Values in italic refer to **MP2**.

Table (27): Dipole moment in gas, water (w), and CCl_4, entropy **S**, zero point energy **ZPE**, thermal correction **TC**, energy gap ΔE_g, E_{HOMO} and E_{LUMO} and Mülliken charges of **2ATH**, and **5-substituted-2ATH** calculated at the **B3LYP** and **MP2 / 6-311++G****.

PARAMETERS	2ATH (1)	5-F (2)	5-Cl (3)	$5-CH_3$ (4)	5-CHO (5)	$5-NO_2$ (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	Ts (2)	Ts (3)	Ts (4)	Ts (5)	Ts (6)
ZPE	45.02	39.97	39.13	62.41	50.69	46.34	44.76	39.62	38.91	62.25	50.83	46.54	36.23	35.35	58.60	47.08	42.89
K cal/mol	*45.37*	*40.41*	*39.53*	*63.10*	*51.16*	*47.08*	*44.43*	*39.99*	*39.12*	*62.76*	*50.52*	*46.45*	*36.86*	*36.00*	*59.61*	*47.58*	*43.52*
TC	48.42	43.93	43.31	66.86	55.44	51.44	48.15	43.64	43.09	66.66	55.43	51.45	40.04	39.43	62.95	51.67	47.75
K cal/mol	*48.77*	*44.34*	*43.71*	*67.59*	*55.93*	*52.16*	*47.58*	*43.93*	*43.30*	*67.22*	*55.48*	*51.67*	*40.53*	*39.91*	*63.81*	*52.13*	*48.37*
S	74.30	79.25	82.00	82.20	85.70	89.28	74.49	80.12	82.33	82.25	85.18	88.31	78.53	81.77	81.86	85.11	87.98
Cal mol^{-1}	*74.44*	*79.15*	*82.12*	*82.70*	*86.29*	*90.04*	*72.81*	*79.48*	*82.49*	*82.81*	*89.08*	*92.10*	*77.66*	*80.58*	*80.94*	*84.93*	*88.41*
E_{HOMO}	-6.074	-6.196	-6.161	-5.859	-6.553	-6.988	-5.704	-5.880	-5.889	-5.548	-6.280	-6.721					
eV	*-8.536*	*-8.811*	*-8.648*	*-8.267*	*-8.977*	*-9.660*	*-8.085*	*-8.455*	*-8.340*	*-7.946*	*-8.574*	*-9.151*					
E_{LUMO}	-0.629	-0.827	-0.920	-0.555	-2.109	-2.895	-0.411	-0.792	-0.697	-0.438	-2.223	-3.031					
eV	*1.113*	*1.012*	*0.996*	*1.086*	*0.846*	*0.672*	*0.901*	*0.939*	*0.933*	*0.909*	*0.922*	*0.664*					
ΔE_g	5.445	5.369	5.241	5.304	4.444	4.093	5.293	5.088	5.192	5.110	4.057	3.69					
eV	*9.649*	*9.823*	*9.644*	*9.353*	*9.823*	*10.332*	*8.986*	*9.394*	*9.273*	*8.855*	*9.496*	*9.815*					
IP	6.074	6.196	6.161	5.859	6.553	6.988	5.704	5.880	5.889	5.548	6.280	6.721					
eV	*8.536*	*8.811*	*8.648*	*8.267*	*8.977*	*9.660*	*8.085*	*8.455*	*8.340*	*7.946*	*8.574*	*9.151*					
Dipole Moment D																	
D.M(gas)	1.705	2.487	2.504	1.617	5.564	6.736	2.728	1.604	1.740	3.173	1.627	4.210	0.695	0.658	1.760	3.925	5.504
	1.762	*2.131*	*2.049*	*1.830*	*4.497*	*5.038*	*2.807*	*1.481*	*1.724*	*3.194*	*0.928*	*3.224*	*0.713*	*0.720*	*2.331*	*2.935*	*4.024*
D.M(W)	2.293	3.309	3.356	2.291	7.533	9.281	3.678	2.175	2.333	4.304	2.226	6.131	0.937	0.975	2.413	5.445	8.008
D.M(CCL_4)	1.928	2.828	2.867	1.860	6.395	7.800	3.143	1.858	2.002	3.664	1.885	4.971	0.791	0.791	2.036	4.565	6.519

Values in italic refer to **MP2**.

Table (27): Continue.

Charge	2ATH (1)	5-F (2)	5-Cl (3)	5-CH_3 (4)	5-CHO (5)	5-NO_2 (6)	23ITH (1)	Imino (2)	Imino (3)	Imino (4)	Imino (5)	Imino (6)	Ts (2)	Ts (3)	Ts (4)	Ts (5)	Ts (6)
N_3	-0.146	-0.146	-0.135	-0.127	-0.128	-0.153	-0.069	-0.081	-0.117	-0.113	-0.113	-0.107	-0.137	-0.161	-0.150	-0.146	-0.165
	-0.116	*-0.112*	*-0.104*	*-0.100*	*-0.093*	*-0.111*	*-0.109*	*-0.083*	*-0.119*	*-0.117*	*-0.157*	*-0.151*	*-0.076*	*-0.092*	*-0.084*	*-0.099*	*-0.118*
C_4	-0.295	-0.046	-0.428	-0.500	-0.243	0.119	-0.204	0.016	-0.294	-0.277	-0.022	0.295	-0.094	-0.440	-0.450	-0.258	0.062
	-0.283	*-0.059*	*-0.381*	*-0.439*	*-0.209*	*0.084*	*-0.187*	*-0.020*	*-0.287*	*-0.274*	*-0.005*	*0.238*	*-0.107*	*-0.397*	*-0.435*	*-0.267*	*-0.054*
C_5	-0.143	-0.184	-0.119	0.458	0.338	-0.355	-0.217	-0.270	-0.244	0.268	0.143	-0.562	-0.195	-0.137	0.392	0.350	-0.398
	-0.211	*-0.201*	*-0.148*	*0.354*	*0.213*	*-0.391*	*-0.261*	*-0.235*	*-0.211*	*0.244*	*0.065*	*-0.557*	*-0.196*	*-0.124*	*0.349*	*0.239*	*-0.334*
N_6	-0.214	-0.219	-0.204	-0.223	-0.213	-0.213	-0.342	-0.336	-0.320	-0.339	-0.309	-0.302	-0.410	-0.414	-0.429	-0.445	-0.434
	-0.285	*-0.294*	*-0.280*	*-0.298*	*-0.282*	*-0.275*	*-0.353*	*-0.337*	*-0.320*	*-0.340*	*-0.311*	*-0.305*	*-0.427*	*-0.419*	*-0.441*	*-0.428*	*-0.417*
H_7	0.257	0.258	0.258	0.258	0.272	0.277	0.317	0.321	0.329	0.331	0.344	0.341	0.326	0.342	0.346	0.382	0.377
	0.266	*0.267*	*0.267*	*0.268*	*0.277*	*0.278*	*0.333*	*0.310*	*0.320*	*0.323*	*0.356*	*0.352*	*0.307*	*0.313*	*0.317*	*0.342*	*0.343*

Values in italic refer to **MP2**.

The electron donating character of these derivatives has the order, (according to their IP values) (8.313 eV) **4CH$_3$** > (8.536 eV) **4H** > (8.689 eV) **4Cl** > (8.778 eV) **4F** > (8.923 eV) **4CHO** > (9.508 eV) **4NO$_2$** (MP2 results).

(3) The energy gap ΔE_g has its maximum value for $–NO_2$ substituent, while that of –Cl derivative is nearly equal to that of the parent **2ATH**.

(ΔE_g) (10.275 eV) **4NO$_2$** > (9.835 eV) **4CHO** > (9.752 eV) **4F** > (9.680 eV) **4Cl** > (9.649 eV) **4H** > (9.423 eV) **4CH$_3$**.

This means that these substituents in position four decrease the reactivity of **2ATH**, except of $–CH_3$ group.

(4) ΔE_g and IP of 4-substituted **2ATH** are greater than that of the corresponding imino forms.

In case of substitution in C_5, the following comments are noticed.

(1) The substituent position does not affect values or trend of IP or E_{HOMO}, while E_{LUMO} values have the same trend of 4-position except of –Cl, and –F.

(2) ΔE_g of **2ATH** is higher than that of 5-CH_3 derivative and equal to that of 5-Cl one at MP2 level, while the other three electron withdrawing groups have higher values. According to that, the reactivity of **5-CH$_3$-2ATH** is higher than **2ATH** and the other derivatives. The charges on C_5 and C_4 in case of **5-CH$_3$-2ATH** indicate its higher reactivity for nucleophilic and electrophilic substitutions, respectively.

(3) The dipole moment of 5-substituted derivatives (–F and –Cl) (amino and imino) is less than that of 4-substituted, in gas and solution phases, but they have the same dipole moment trends.

4.3.1.3. ***ENERGIES AND RELATIVE STABILITIES***

Tables (28-31) list the gas phase total energy, conversion barrier, activation energy, reaction enthalpy, energy difference, Gibbs free energy and equilibrium constant of 5- and 4-substituted 2-aminothiazole and the corresponding 2(3H)-imino tautomer.

One can notice the followings:

(1) 4-Me, 4-F and 4-Cl isomers are more stable than their 5-isomers while the reverse is found in case of nitro and formyl isomers. Both latter groups in 5-position participate in the ring delocalization, while in 4-position they don't involve.

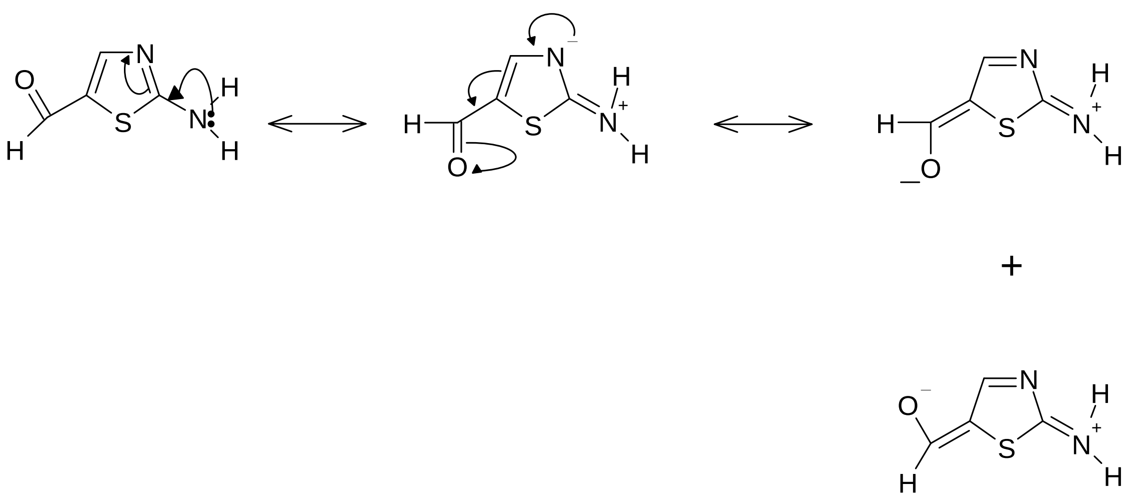


Table (28): Total energy in gas, water (w), and CCl_4 of **2ATH**, and **4-substituted-2ATH** calculated at the **B3LYP** and **MP2 6-311++G****.

Total Energy a.u.	E_t (gas)	E_t (w)	E_t (CCl_4)
2ATH (1)	-624.50691 *-623.45805*	-624.51708	-624.51124
4-F (2)	-723.77504 *-722.56086*	-723.78669	-723.78002
4-Cl (3)	-1084.12892 *-1082.56890*	-1084.14001	-1084.13362
4-CH_3 (4)	-663.83896 *-662.68245*	-663.84880	-663.84310
4-CHO (5)	-737.86677 *-736.58667*	-737.88116	-737.87301
4-NO_2 (6)	-829.06779 *-827.63245*	-829.08686	-829.07591
23ITH (1)	-624.49454 *-623.43856*	-624.50592	-624.4994
Imino (2)	-723.75646 *-722.53617*	-723.76649	-723.76081
Imino (3)	-1084.11307 *-1082.5469*	-1084.12231	-1084.11705
Imino (4)	-663.82703 *-662.66368*	-663.83857	-663.83198
Imino (5)	-737.85076 *-736.56299*	-737.86559	-737.85700
Imino (6)	-829.05483 *-827.61150*	-829.06894	-829.06076
TS (2)	-723.68423 *-722.46868*	-723.68995	-723.68665
TS (3)	-1084.03970 *-1082.47895*	-1084.04506	-1084.04193
TS (4)	-663.75287 *-662.59508*	-663.75858	-663.75526
TS (5)	-737.77693 *-736.49598*	-737.78662	-737.78105
TS (6)	-828.97726 *-827.54121*	-829.98971	-829.98251

Values in italic refer to **MP2**.

Table (29): Total energy in gas, water (w), and CCl_4 of **2ATH**, and **5-substituted-2ATH** calculated at the **B3LYP** and **MP2 6-311++G****.

Total Energy a.u.	E_t **(gas)**	E_t **(w)**	E_t **(CCl_4)**
2ATH (1)	-624.50691	-624.51708	-624.51124
	-623.45805		
5-F (2)	-723.76159	-723.77157	-723.76585
	-722.54740		
5-Cl (3)	-1084.12339	-1084.13296	-1084.12748
	-1082.56245		
5-CH_3 (4)	-663.83642	-663.84684	-663.84082
	-662.68049		
5-CHO (5)	-737.86752	-737.88386	-737.87450
	-736.58412		
5-NO_2 (6)	-829.06850	-829.08687	-829.07643
	-827.62806		
23ITH (1)	-624.49454	-624.50592	-624.4994
	-623.43856		
Imino (2)	-723.74878	-723.75954	-723.75341
	-722.52769		
Imino (3)	-1084.11044	-1084.12083	-1084.11491
	-1082.54290		
Imino (4)	-663.82503	-663.83629	-663.82985
	-662.66201		
Imino (5)	-737.85592	-737.87216	-737.86287
	-736.56673		
Imino (6)	-829.05619	-829.07510	-829.06418
	-827.61083		
TS (2)	-723.67498	-723.6806	-723.67737
	-722.46014		
TS (3)	-1084.03695	-1084.04203	-1084.03909
	-1082.47505		
TS (4)	-663.75008	-663.75602	-663.75256
	-662.59321		
TS (5)	-737.78432	-737.79587	-737.78921
	-736.49834		
TS (6)	-828.98587	-829.00011	-828.99187
	-827.54292		

Values in italic refer to **MP2**.

Table (30): Relative stabilities conversion barrier **ΔE*(**kcal/mol), activation energy $\mathbf{E_a}$ (kcal/mol), reaction enthalpy **ΔH** (kcal/mol), and Gibbs free energy **ΔG** (Kcal/mol), and equilibrium constant **K** of **2ATH**, and **4-Substituted-2ATH** calculated at the **B3LYP** and **MP2 / 6-311++G****.

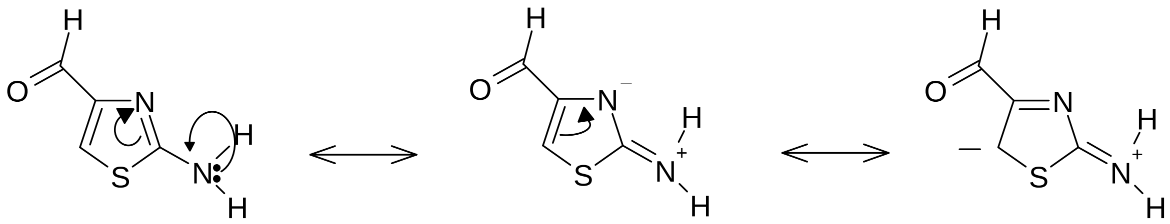
	2ATH	2ATH-4F	2ATH-4Cl	2ATH-4CH$_3$	2ATH-4CHO	2ATH-4NO$_2$
ΔE*	54.34 *55.18*	56.98 *57.84*	55.99 *56.44*	54.02 *54.82*	56.37 *56.91*	56.81 *57.25*
Ea	46.64 *48.26*	49.83 *51.26*	48.77 *49.75*	47.06 *48.27*	49.38 *50.06*	49.64 *50.62*
ΔE	7.76 *12.23*	11.66 *15.49*	9.95 *13.83*	7.49 *11.78*	10.05 *14.86*	8.13 *13.15*
ΔH	7.23 *10.10*	11.14 *14.70*	9.45 *13.19*	7.18 *11.36*	9.75 *18.21*	7.50 *13.15*
ΔG	7.18 *10.59*	10.94 *14.60*	9.26 *13.01*	6.95 *11.41*	9.65 *18.98*	7.65 *13.48*
LogK	-5.2593 *-7.7590*	-8.0157 *-10.6979*	-6.7879 *-9.5322*	-5.0958 *-8.3621*	-7.0736 *-13.9080*	-5.6060 *-9.8820*
K	1.82×10^{5} 5.74×10^{7}	1.04×10^{8} 4.99×10^{10}	6.14×10^{6} 3.41×10^{9}	1.25×10^{5} 2.30×10^{8}	1.18×10^{7} 8.09×10^{13}	4.04×10^{5} 7.62×10^{9}

Values in italic refer to **MP2**.

Table (31): Relative stabilities conversion barrier **ΔE*(**kcal/mol), activation energy $\mathbf{E_a}$ (kcal/mol), reaction enthalpy **ΔH** (kcal/mol), and Gibbs free energy **ΔG** (Kcal/mol), and equilibrium constant **K** of **2ATH**, and **5-Substituted-2ATH** calculated at the **B3LYP** and **MP2 / 6-311++G****.

	2ATH	2ATH-5F	2ATH-5Cl	2ATH-5CH$_3$	2ATH-5CHO	2ATH-5NO$_2$
ΔE*	54.34 *55.18*	54.35 *54.76*	54.24 *54.84*	54.18 *54.77*	52.21 *53.83*	51.85 *53.43*
Ea	46.64 *48.26*	47.31 *47.99*	47.17 *48.11*	47.05 *48.09*	45.42 *47.04*	45.30 *46.67*
ΔE	7.76 *12.23*	8.04 *12.37*	8.13 *12.27*	7.15 *11.60*	7.28 *10.91*	7.72 *10.81*
ΔH	7.23 *10.10*	7.40 *11.54*	7.69 *11.45*	6.79 *10.89*	7.41 *9.82*	7.93 *9.69*
ΔG	7.18 *10.59*	7.14 *11.44*	7.59 *11.34*	6.77 *10.85*	7.56 *8.99*	8.22 *9.08*
LogK	-5.2593 *-7.7590*	-5.2324 *-8.3847*	-5.5614 *-8.3097*	-4.9638 *-7.9550*	-5.5440 *-6.5895*	-6.0276 *-6.6534*
K	1.82×10^{5} 5.74×10^{7}	1.71×10^{5} 2.42×10^{8}	3.64×10^{5} 2.04×10^{8}	9.20×10^{4} 9.02×10^{7}	3.50×10^{5} 3.89×10^{6}	1.07×10^{6} 4.50×10^{6}

Values in italic refer to **MP2**.



(2) In all cases, the amino form is more stable than its imino form leading to endothermic enthalpy, as in case of the unsubstituted **2ATH**, i.e. the type and position of ring substituent do not affect the relative stability of amino and imino tautomers. This is in agreement with the available experimental data(37,70,176). The reaction enthalpy ΔH and Gibbs free energy ΔG for 4-derivative tautomerization are more positive than for 5-isomers i.e. more endothermic process. This means less imino amount in case of 4-isomers. The lowest value of ΔG is for 4-CH_3 substitution and the highest one is for 4-F derivative. The following trend is calculated for ΔH, ΔG (more positive) for the 4-isomer series:

$4CH_3$ < H < $4NO_2$ < 4Cl < 4CHO < 4F (B3LYP)

H < $4CH_3$ < $4NO_2$< 4Cl < 4F < 4CHO (MP2)

while for the other series, the trend becomes:

$5CH_3$ < H < 5F < 5CHO < 5Cl < $5NO_2$ (B3LYP)

5CHO < $5NO_2$ < H < $5CH_3$ < 5Cl < 5F (MP2)

This means that electron donating group (-CH_3) at the positions four and five increases the imino amount, while the electron withdrawing groups reduce the imino amounts.

(3) The activation energy E_a increases upon 4-substitution and has its minimum for 4-CH_3. The 5-position isomers have E_a less than 4-isomer ones. The order of E_a in the two series is

(4-position) **H < 4CH_3 < 4Cl < 4CHO < 4NO_2 < 4F** (B3LYP)

(4-position) **H < 4CH_3 < 4Cl < 4CHO < 4F < 4 NO_2** (MP2)

(5-position) **5NO_2 < 5CHO < H < 5CH_3 < 5Cl < 5F** (B3LYP)

(5-position) **5NO_2 < 5CHO < 5F < 5CH_3 < 5Cl < H** (MP2)

(4) The entropy change ΔS is very low, therefore, the enthalpy change ΔH represents the main contribution for the Gibbs free energy ΔG.

4.3.1.4. ***SOLVENT EFFECT :***

Tables (26 and 27) show the dipole moment of 4-derivatives and their 5-isomers (amino and imino) in gas, water, and CCl_4 phases. The dipole moment of any form in gas phase is less than in the two solutions, while the highest dipole moment is that in water. On the other hand, the dipole moment of imino form is less than that of amino tautomer except of –CH_3 derivative. The dipole moment of 4-CH_3 derivative is 1.327 D i.e. less than that of **2ATH**, while the other substituents increase the dipole moment. Therefore, the dipole vector of this substituent is alined with that of nitrogen lone pairs. The dipole moment order of gas phase form of the 4-substituted 2-aminothiazole is:

(6.722 D) **4NO$_2$** > (4.962 D) **4CHO** > (3.543 D) **4F** > (3.416 D) **4Cl** > (1.705 D) **4H** > (1.327 D) **4CH$_3$** (B3LYP results), while that of thiazole-2(3H)-imino **23ITH** forms is:

(3.494 D) **4NO$_2$** > (3.232 D) **4CH$_3$** > (2.728 D) **4H** > (1.608 D) **4Cl** > (1.359 D) **4F** > (0.925 D) **4CHO** at the same level. Therefore, it is expected to find different effects on equilibrium ratio in different media. The order of dipole moment of 5-substituted **2ATH** is:

(6.736 D) **5NO$_2$** > (5.564 D) **5CHO** > (2.504 D) **5Cl** > (2.487 D) **5F** > (1.705 D) **5H** > (1.617 D) **5CH$_3$** and that of the corresponding imino forms is (4.210 D) **5NO$_2$** > (3.173 D) **5CH$_3$** > (2.728 D) **5H** > (1.740 D) **5Cl** > (1.627 D) **5CHO** > (1.604 D) **5F**, at B3LYP method. As in case of the parent, the two solvents increase the dipole moment of both tautomers with higher extent for amino one.

The total energy of the studied derivatives in gas phase and in the two solutions are given in Tables (28 and 29). All compounds have the lowest energy in both water and CCl_4 solvents and the highest at the gas phase i.e. they are more stabilized in solutions. The calculated solvation free energy G^o_s, relative solvation free energy ΔG^o_s and relative free energy in solution ΔG^o_{soln} for 4- and 5-substituted tautomers at B3LYP/6-311++G** are collected in Table (32). The 5-derivative imino tautomers are more solvated than their amino forms. This explains the decrease of

their relative Gibbs free energy in solutions than in gas phase. Yet, this does not affect the relative stability of amino and imino forms and therefore, the amino form is still the main tautomer in both solutions. The only change is the decrease of equilibrium constant K value comparing to its value in gas phase. The relative Gibbs free energy of 4-isomers in both solutions become higher than that in gas phase, that's due to the more stabilization of amino form over its imino in the two solutions, except in case of 4-CHO and 4-CH_3.

Table (32): The solvation energy G_s°, the free energy of solvation ΔG_s°, the relative free energy in the solvents ΔG_{soln}°, the relative free energy in gas phase ΔG_g°, the equilibrium constants K_{soln} in water (w) and CCl_4 and the equilibrium constants K_g in gas phase of **4-**, **5- and 2-substituted-2ATH** and their tautomers calculated at the **B3LYP / 6-311++G****.

Tautomers	G°_s Kcal/mol	ΔG°_s Kcal/mol	ΔG°_g Kcal/mol	ΔG°_{soln} Kcal/mol	K_{soln}	K_g
4F-2ATH						
(w)	-7.31	0.0				
(CCl_4)	-3.12	0.0				
4F-23ITH			10.94			1.04×10^{8}
(w)	-6.29	1.02		11.96	5.84×10^{8}	
(CCl_4)	-2.73	0.39		11.33	2.02×10^{8}	
4Cl-2ATH						
(w)	-6.96	0.0				
(CCl_4)	-2.95	0.0				
4Cl-23ITH			9.26			6.14×10^{6}
(w)	-5.80	1.16		10.42	4.34×10^{7}	
(CCl_4)	-2.50	0.45		9.71	1.31×10^{7}	
$4CH_3$-2ATH						
(w)	-6.17	0.0				
(CCl_4)	-2.60	0.0				
$4CH_3$-23ITH			6.95			1.25×10^{5}
(w)	-7.24	-1.07		5.88	2.04×10^{4}	
(CCl_4)	-3.11	-0.51		6.44	5.25×10^{4}	
4CHO-2ATH						
(w)	-9.03	0.0				
(CCl_4)	-3.92	0.0				
4CHO-23ITH			9.65			1.18×10^{7}
(w)	-9.31	-0.28		9.37	7.37×10^{6}	
(CCl_4)	-3.92	0.0		9.65	1.18×10^{7}	
4-NO_2-2ATH						
(w)	-11.97	0.0				
(CCl_4)	-5.10	0.0				
4-NO_2-23ITH			7.65			4.04×10^{5}
(w)	-8.85	3.12		10.77	7.83×10^{7}	
(CCl_4)	-3.72	1.38		9.03	4.15×10^{6}	
5F-2ATH						
(w)	-6.26	0.0				
(CCl_4)	-2.67	0.0				
5F-23ITH						
(w)	-6.75	-0.49	7.14	6.65	7.48×10^{4}	1.71×10^{5}
(CCl_4)	-2.91	-0.24		6.90	1.14×10^{5}	

Table (32): Continue.

Tautomers	G°_{s} Kcal/mol	ΔG°_{s} Kcal/mol	ΔG°_{g} Kcal/mol	ΔG°_{soln} Kcal/mol	K_{soln}	K_{g}
5Cl-2ATH						
(w)	-6.01	0.0				
(CCl_4)	-2.57	0.0				
5Cl-23ITH			7.59			3.64×10^{5}
(w)	-6.52	-0.51		7.08	1.55×10^{5}	
(CCl_4)	-2.80	-0.23		7.36	2.48×10^{5}	
$5CH_3$-2ATH						
(w)	-6.54	0.0				
(CCl_4)	-2.76	0.0				
$5CH_3$-2ATH						
(w)	-6.54	0.0				
(CCl_4)	-2.76	0.0				
$5CH_3$-23ITH			6.77			9.20×10^{4}
(w)	-7.07	-0.53		6.24	3.75×10^{4}	
(CCl_4)	-3.02	-0.26		6.51	5.91×10^{4}	
5CHO-2ATH						
(w)	-10.25	0.0				
(CCl_4)	-4.38	0.0				
5CHO-23ITH			7.56			3.50×10^{5}
(w)	-10.19	0.06		7.62	3.85×10^{5}	
(CCl_4)	-4.36	0.02		7.58	3.60×10^{5}	
5-NO_2-2ATH						
(w)	-11.53	0.0				
(CCl_4)	-4.98	0.0				
5-NO_2-23ITH			8.22			1.07×10^{6}
(w)	-11.87	-0.34		7.88	5.97×10^{5}	
(CCl_4)	-5.01	-0.03		8.19	1.01×10^{6}	
N-NO_2-2ATH						
(w)	-7.57	0.0				
(CCl_4)	-3.25	0.0				
N-NO_2-23ITH			0.05			1.109
(w)	-13.84	-6.27		-6.22	2.76×10^{-5}	
(CCl_4)	-5.91	-2.66		-2.61	1.22×10^{-2}	

4.3.2. N-SUBSTITUTED 2-AMINOTHIAZOLE

4.3.2.1. *GEOMETRY*

Experimentally the substitution of **2ATH** by an electron-withdrawing group at the exocyclic nitrogen stabilizes the imino form[42]. To understand the effect of such groups on stabilizing **23ITH** form we extend our study by performing the MO calculations on 2-(N-nitro-amino)thiazole using B3LYP/6-311++G** method. The presence of a nitro group (strong electron withdrawing group) attached to the exocyclic nitrogen slightly elongates the C_2N_3 bond and shortens the two CS bonds comparing to the **2ATH** itself, Table (33). This means that an increase in extent of conjugation of lone pair of exocyclic nitrogen with the thiazole cycle occurs. In case of the imino tautomer, all single bonds shorten while the double bonds elongate comparing to **NNO_2-2ATH** indicating that nitrogen atom lone pair participates in ring resonance more than in case of **23ITH**. In addition, the acidity of exocyclic $-NH_2$ increases, the positive charge of hydrogen atom is 0.326 i.e. it increases by 0.07 more than that in case of the unsubstituted **2ATH**, which facilitates its transfer to the endocyclic nitrogen atom N_3.

Table (33): Geometrical parameters of **2ATH** and **NNO_2-2ATH** calculated at the **B3LYP / 6-311++G**.**

Bond Length Å (Bond Order)	2ATH	NNO_2-2ATH	23ITH	Imino	TS
S_1C_2	1.767 (0.996)	1.748 (1.064)	1.809 (0.907)	1.763 (1.044)	1.714 (1.178)
S_1C_5	1.749 (1.027)	1.740 (1.041)	1.768 (0.965)	1.763 (0.991)	1.766 (1.031)
C_2N_3	1.298 (1.758)	1.299 (1.781)	1.385 (1.140)	1.360 (1.292)	1.327 (1.428)
C_2N_6	1.377 (1.163)	1.394 (0.961)	1.272 (1.893)	1.312 (1.355)	1.360 (1.080)
N_3C_4	1.379 (0.930)	1.375 (0.943)	1.385 (0.863)	1.386 (0.863)	1.376 (0.990)
C_4C_5	1.356 (1.908)	1.360 (1.846)	1.341 (2.101)	1.343 (2.081)	1.358 (1.920)
N_6X_8	1.009 (0.905)	1.378 (0.831)	1.015 (0.852)	1.380 (0.818)	1.372 (0.843)
N_6H_7	1.011 (0.934)	1.013 (0.880)	2.571 ---	2.501 ---	1.380 (0.403)
H_7O_{11}	---	3.083	---	4.627	3.548

Values between parentheses refer to **Bond Order.**

Table (33): Continue.

Bond Angles *Dihedral Angles* degree	**2ATH**	**NNO_2-2ATH**	**23ITH**	**Imino**	**TS**
$N_3C_2S_1$	114.8	116.0	106.4	109.2	114.5
$N_3C_2S_1N_6$	*176.4*	*-176.7*	*180.0*	*180.0*	*-173.5*
$C_4N_3C_2$	110.8	110.1	117.0	116.0	112.8
$C_4N_3C_2S_1$	*0.1*	*-177.0*	*0.0*	*0.0*	*-173.2*
$C_5C_4N_3$	116.7	81.5	114.2	112.6	87.9
$C_5C_4N_3C_2$	*0.4*	*-175.2*	*0.0*	*0.0*	*-175.9*
$N_6C_2S_1$	121.1	125.2	130.4	132.0	141.8
$N_6C_2S_1N_3$	*176.4*	*-176.7*	*180.0*	*180.0*	*-173.5*
$H_7N_6C_2$	113.4	117.7	118.7	119.4	78.6
$H_7N_6C_2N_3$	*15.4*	*-8.5*	*0.0*	*0.0*	*2.7*
$X_8N_6C_2$	117.3	125.0	113.2	116.1	121.3
$X_8N_6C_2N_3$	*151.9*	*-164.0*	*180.0*	*180.0*	*-157.7*

Values in italic refer to **Dihedral Angles**.

4.3.2.2. ***IONIZATION POTENTIAL***

Table (34) shows the E_{HOMO} and E_{LUMO} for **2ATH**, **NNO_2-2ATH** and the corresponding 2(3H)-imino tautomers. The IP of **NNO_2-2ATH** is higher than its parent i.e. NO_2 group stabilizes the HOMO and also LUMO. This is reflected on the value of ΔE_g which is less by 0.92 eV than that of **2ATH** i.e. it is more reactive. The order of IP is (7.070 eV) **NNO_2-2ATH** > (6.074 eV) **2ATH**

(ΔE_g) (5.445 eV) **2ATH** > (4.526 eV) **NNO_2-2ATH**

In addition, the presence of NO_2 group duplicates the dipole moment of amino tautomer, and increases that of its imino form by three times. This means that the later will be more stabilized in more polar solvents than the amino form, Table (34).

(Dipole Moment) (8.212 D) **NNO_2-23ITH** > (3.470 D) **NNO_2-2ATH** > (1.705 D) **2ATH**.

4.3.2.3. ***ENERGIES AND RELATIVE STABILITY***

Tables (34 and 35) collect the energies and thermodynamic data for the tautomerism **NNO_2-2ATH** $\rightleftharpoons$ **NNO_2-23ITH**. The imino **NNO_2-23ITH** total energy is less than **NNO_2-2ATH** by only 0.00065 a.u. (0.41 Kcal/mol) i.e. in gas phase the imino is more stable by only 0.41 Kcal/mol. The data also shows a decrease in reaction activation energy E_a by 6.65 Kcal/mol comparing to **2ATH**. Consequently, the process becomes easier.

Table (34): Total energy in gas, water (w), and CCl_4, net charges, Ionization Potential **IP**, energy gap ΔE_g, dipole moment in gas, water, and CCl_4 of **2ATH** and **NNO_2-2ATH** calculated at the **B3LYP /6-311++G****.

Parameter	2ATH	NNO_2-2ATH	23ITH	Imino	TS
E_t(gas) a.u.	-624.50691	-829.04385	-624.49454	-829.04450	-828.96950
ZPE	45.02 k	46.65	44.76	46.66	43.06
TC	48.42	51.39	48.15	51.32	47.72
S	74.30 cal	88.28	74.49	86.53	87.74
E_{HOMO} eV	-6.074	-7.070	-5.704	-6.885	
E_{LUMO} eV	-0.629	-2.544	-0.411	-2.223	
ΔE_g eV	5.445	4.526	5.293	4.662	
IP eV	6.074	7.070	5.704	6.885	
E_t(W)	-624.51708	-829.05592	-624.50592	-829.06655	-828.98394
E_t(CCL_4)	-624.51124	-829.04903	-624.49940	-829.05392	-828.97572
Dipole Moment D					
D.M (gas)	1.705	3.470	2.728	8.212	6.803
D.M (W)	2.293	4.676	3.678	11.529	9.387
D.M (CCL_4)	1.928	3.992	3.143	9.605	7.907
Charge					
N_3	-0.146	-0.087	-0.069	-0.075	-0.087
C_4	-0.295	-0.304	-0.204	-0.146	-0.287
C_5	-0.143	-0.100	-0.217	-0.264	-0.168
N_6	-0.214	0.052	-0.342	-0.004	-0.061
H_7	0.257	0.326	0.317	0.333	0.383
X_8	0.245	-0.166	0.222	-0.316	-0.243

Zero point energy **ZPE**, thermal correction **TC** Kcal/mol, and entropy **S** cal/mol-K.

Table (35): Relative stabilities conversion barrier **ΔE***(kcal/mol), activation energy **E_a**(kcal/mol), reaction enthalpy **ΔH** (kcal/mol), and Gibbs free energy change **ΔG** (Kcal/mol), and equilibrium constant **K** of **2ATH** and **NNO_2-2ATH** calculated the **B3LYP / 6-311++G****.

parameter	2ATH=23ITH	NNO_2-2ATH
ΔE*	54.34	46.65
Ea	46.64	39.99
ΔE	7.76	-0.41
ΔH	7.23	-0.47
ΔG	7.18	0.05
LogK	-5.26	-0.0395
K	1.82×10^5	1.109

The enthalpy of tautomerization process ΔH is found to be so low exothermic (-0.47 Kcal/mol), while the Gibbs free energy ΔG is 0.05 Kcal/mol. These data prove that the two forms coexist in the gas phase. Therefore, the two compounds are of nearly equal amounts (K=1.109) while, that of the unsubstituted **2ATH** is ($K=1.82\times10^{5}$) i.e. only the amino exists. This is in good agreement with the available experimental data[42] which confirm the existence of 2-p-tosylaminothiazole mainly as imino structure.

4.3.2.4. ***SOLVENT EFFECT***

The N-substitution largely increases the gaseous dipole moment of **NNO_2-2ATH** and **NNO_2-23ITH** comparing to the unsubstituted forms, which means a pronounced solvent effect on both tautomers specially in polar medium. The total energy of the two compounds in water and carbon tetrachloride solutions decreases i.e. more stabilized than in gas phase where the imino form (higher dipole moment) is more stabilized than the amino form **NNO_2-2ATH** in the two solvents. The relative free energy in both solutions are -6.22 and -2.61 Kcal/mol i.e. the tautomerization becomes spontaneous in solutions at room temperature, Table (32). The equilibrium constants are 2.76×10^{-5} and 1.22×10^{-2} in H_2O and CCl_4, respectively. In solution, **NNO_2-23ITH** is more predominant.

4.3.3. SUBSTITUTED 4-AMINOTHIAZOLE

4.3.3.1. <u>*GEOMETRY*</u>

Table (36) presents the calculated geometrical parameters of **2X-** and **5X-4ATH** and their imino forms, where X= –F or $–CH_3$. The electron with drawing group (-F) in position two elongates the two single bonds C_4N_3 and C_5S_1, while C_4N_6 bond shortens by 0.003Å. This lead to less participating of exocyclic nitrogen lone pair into delocalization of the ring. On other hand, the $–CH_3$ group affects only CS bond (elongate). The geometry of **2X-4ATH** and **4X-2ATH** are very different in bond lengths. The substitution of **4ATH** in position five has little effect in its geometry comparing to that in position two.

4.3.3.2. <u>*ENERGIES AND RELATIVE STABILITY*</u>

The total energy of substituted **4ATH** is higher than the corresponding substituted **2ATH**. The same trend is also found for the two parent isomers **2ATH** and **4ATH**. The stability of **2X-4ATH** is higher than that of **5X-4ATH**, the difference is 0.0118 a.u. and 0.00448 a.u. for X = F and CH_3, respectively. The tautomerization process is endothermic due to the less stability of imino structures than its amino ones. The enthalpy of reaction of 2- and 5-fluoro derivatives is nearly the same (3.57 and 3.91 Kcal/mol) and is less than that of methyl derivatives

Table (36): Geometrical parameters of **2- and 5-Substituted (F, CH3)-4ATH** calculated at the **B3LYP/6-311++G**.**

Bond length Å (Bond Order)	2-F (1)	2-CH3 (2)	5-F (3)	5-CH3 (4)	Imino (1)	Imino (2)	Imino (3)	Imino (4)	TS (1)	TS (2)	TS (3)	TS (4)
S_1C_2	1.735 (1.103)	1.749 (1.170)	1.744 (1.100)	1.736 (1.133)	1.761 (0.995)	1.787 (1.021)	1.777 (1.015)	1.761 (1.025)	1.753 (1.114)	1.770 (1.132)	1.754 (1.188)	1.751 (1.172)
S_1C_5	1.752 (0.833)	1.738 (0.900)	1.740 (0.928)	1.747 (0.820)	1.839 (0.735)	1.828 (0.841)	1.827 (0.886)	1.849 (0.686)	1.826 (0.849)	1.808 (0.941)	1.839 (0.899)	1.822 (0.849)
CX_9	1.329 (1.037)	1.492 (0.650)	1.345 (1.227)	1.497 (0.204)	1.323 (1.082)	1.494 (0.643)	1.389 (1.328)	1.529 (0.829)	1.320 (1.079)	1.494 (0.717)	1.406 (1.207)	1.530 (0.863)
C_2N_3	1.279 (1.632)	1.301 (1.567)	1.297 (1.548)	1.298 (1.514)	1.265 (1.660)	1.281 (1.657)	1.276 (1.641)	1.279 (1.610)	1.290 (1.527)	1.307 (1.520)	1.306 (1.449)	1.303 (1.445)
N_3C_4	1.385 (1.002)	1.377 (0.980)	1.376 (1.045)	1.377 (1.038)	1.413 (0.959)	1.411 (0.926)	1.413 (1.026)	1.414 (1.087)	1.372 (1.107)	1.367 (1.061)	1.364 (1.161)	1.371 (1.244)
C_4C_5	1.368 (1.895)	1.370 (1.690)	1.364 (1.794)	1.373 (1.746)	1.535 (0.902)	1.532 (0.825)	1.537 (0.918)	1.538 (0.779)	1.459 (1.175)	1.457 (1.132)	1.504 (1.157)	1.461 (1.123)
C_4N_6	1.387 (1.094)	1.392 (1.091)	1.389 (1.176)	1.397 (1.025)	1.264 (2.015)	1.267 (2.004)	1.263 (2.013)	1.268 (2.055)	1.309 (1.559)	1.315 (1.564)	1.296 (1.630)	1.315 (1.579)
N_6H_7	1.009 (0.911)	1.009 (0.913)	1.010 (0.909)	1.010 (0.927)	2.772 ---	2.774 ---	2.699 ---	2.756 ---	1.341 (0.440)	1.346 (0.435)	1.283 (0.439)	1.332 (0.416)
C_5H_7	2.703 ---	2.706 ---	2.684 ---	2.726 ---	1.089 (0.979)	1.089 (0.973)	1.087 (0.969)	1.091 (0.962)	1.493 (0.438)	1.488 (0.422)	1.547 (0.466)	1.504 (0.454)

Values between parentheses refer to **Bond Order**.

Table (36): Continue.

Bond Angles *Dihedral Angles* degree	2-F (1)	2-CH$_3$ (2)	5-F (3)	5-CH$_3$ (4)	Imino (1)	Imino (2)	Imino (3)	Imino (4)	TS (1)	TS (2)	TS (3)	TS (4)
$X_9C_2S_1$	119.3	122.0	---	---	115.8	118.6	---	---	117.8	120.3	---	---
$X_9C_5S_1N_3$	*179.7*	*-178.3*	---	---	*180.0*	*180.0*	---	---	*176.6*	*-176.1*	---	---
$X_9C_5C_4$	---	---	126.3	128.2	---	---	109.6	112.7	---	---	111.1	119.0
$X_9C_5C_4N_3$	---	---	*179.6*	*178.9*	---	---	*103.5*	*-119.7*	---	---	*96.1*	*106.3*
$N_3C_2S_1$	117.7	114.0	115.8	115.0	122.0	117.8	119.6	119.9	121.2	117.2	120.1	118.9
$N_3C_2S_1X$	*179.7*	*-178.3*	*179.7*	*179.4*	*180.0*	*180.0*	*179.5*	*179.8*	*176.6*	*-176.1*	*176.4*	*177.1*
$C_4N_3C_2$	109.6	111.9	111.7	110.9	116.7	113.2	111.2	111.7	105.9	108.3	106.2	106.9
$C_4N_3C_2S_1$	*0.1*	*0.1*	*0.0*	*0.3*	*0.0*	*0.0*	*1.5*	*0.4*	*-3.0*	*4.5*	*-4.4*	*-4.2*
$C_5C_4N_3$	115.6	115.4	113.3	116.3	113.8	113.7	113.7	114.4	120.2	119.9	121.3	120.3
$C_5C_4N_3C_2$	*0.4*	*0.3*	*0.3*	*0.3*	*0.0*	*0.1*	*11.1*	*-2.7*	*12.9*	*-13.7*	*15.2*	*15.8*
$N_6C_4N_3$	116.8	117.3	119.5	117.8	126.1	125.7	126.5	125.3	132.0	131.9	132.9	130.9
$N_6C_4N_3C_2$	*-176.9*	*-176.9*	*176.8*	*177.4*	*179.9*	*180.0*	*-168.7*	*177.6*	*-153.0*	*151.0*	*-148.7*	*-147.3*
$H_7N_6C_4$	116.0	115.6	115.2	115.4	110.8	110.7	112.7	108.6	70.2	70.2	68.8	69.2
$H_7N_6C_4N_3$	*-157.6*	*-154.9*	*157.7*	*144.2*	*-60.8*	*119.6*	*-136.5*	*117.8*	*6.2*	*162.3*	*-162.9*	*-159.7*

Values in italic refer to **Dihedral Angles.**

(4.09 and 8.70 Kcal/mol). These values are less than for unsubstituted **4ATH**, Table (37). The contribution of entropy is so small, therefore, the gas phase Gibbs free energy ΔG has the same trend of ΔH,

$$\Delta G_{2F\text{-}4ATH} < \Delta G_{2CH_3\text{-}4ATH} < \Delta G_{5F\text{-}4ATH} < \Delta G_{4ATH} < \Delta G_{5CH_3\text{-}4ATH}.$$

The values of ΔG and K of such derivatives indicate an increase of the imino form concentration more than in case of **4ATH**, except for **5CH$_3$-4ATH** derivative. The electron withdrawing group 5-F or 2-F increases the amount of the imino form more than $-CH_3$ group.

4.3.3.3. *IONIZATION POTENTIAL*

Table (38) shows the E_{HOMO}, E_{LUMO} for **2X-4ATH** and **5X-4ATH**tautomers. The data depicted in this table shows that:

(1) The electron withdrawing group (-F) in positions two and five stabilizes the HOMO of **4ATH** by 0.139 and 0.123 Kcal/mol, respectively.

(2) The electron donating group ($-CH_3$) in positions two and five destabilizes the HOMO of the parent **4ATH** by 0.215 and 0.166 Kcal/mol, respectively.

(3) The order of IP for **2X-4ATH**, **5X-4ATH** and **4ATH** tautomers is (6.049 eV) **2F-4ATH** > (6.033 eV) **5F-4ATH** > (5.910 eV) **4ATH** > (5.744 eV) **5CH$_3$ -4ATH** > (5.695 eV) **2CH$_3$-4ATH**.

Table (37): Relative stabilities conversion barrier **ΔE***(kcal/mol), activation energy $\mathbf{E_a}$ (kcal/mol), reaction enthalpy **ΔH** (kcal/mol), and Gibbs free energy change **ΔG** (Kcal/mol), and equilibrium constant **K** of **4ATH**, 2- and 5-substituted -(F, CH_3)-4-aminothiazole calculated at the **B3LYP / 6-311++G**.**

	4ATH	**4ATH-2F**	**4ATH-2CH$_3$**	**4ATH-5F**	**4ATH-5CH$_3$**
ΔE*	71.69	68.06	69.68	72.53	74.64
Ea	64.14	60.68	60.44	64.91	68.15
ΔE	7.42	3.43	5.04	3.79	7.86
ΔH	7.33	3.57	4.09	3.91	8.70
ΔG	7.17	3.44	4.01	4.12	8.02
LogK	-5.2589	-2.5201	-2.9401	-3.0189	-5.8759
K	1.82×10^5	3.31×10^2	8.71×10^2	1.04×10^3	7.51×10^5

Table (38): Total energy in gas, water (w), and CCl_4, net charges, **IP**, energy gap ΔE_g, and Dipole moment in gas, water, and CCl_4 of 2-, 5-substituted 4-aminothiazole calculated at the **B3LYP/6-311++G**.**

Parameter	2-F(1)	2-CH$_3$(2)	5-F(3)	5-CH$_3$(4)	Imino(1)	Imino(2)	Imino(3)	Imino(4)	TS (1)	TS (2)	TS (3)	TS (4)
E_t(g) a.u.	-723.76907	-663.83631	-723.75727	-663.83183	-723.76360	-663.82828	-723.75123	-663.81930	-723.66060	-663.72526	-723.64168	-663.71288
ZPE	39.97	62.14	39.90	62.16	40.12	62.24	40.09	62.50	36.16	58.11	35.93	58.60
TC	43.89	66.65	43.89	66.18	43.88	66.60	43.82	66.68	39.72	61.84	39.64	62.66
S	78.99	83.04	78.57	79.50	79.44	83.30	78.87	81.80	76.92	77.81	78.12	79.81
E_{HOMO} eV	-6.049	-5.695	-6.033	-5.744	-7.374	-6.846	-7.652	-6.966				
E_{LUMO} eV	-0.887	-0.751	-1.127	-0.841	-1.766	-1.646	-2.474	-1.864				
ΔE_g eV	5.162	4.944	4.906	4.903	5.608	5.200	5.178	5.102				
IP eV	6.049	5.695	6.033	5.744	7.374	6.846	7.652	6.966				
Dipole Moment D												
D.M(gas)	2.969	1.142	1.087	1.844	1.895	2.709	2.700	2.004	1.425	1.532	2.590	0.757
D.M(W)	3.906	1.687	1.398	2.565	2.622	3.776	3.601	2.893	1.988	1.910	3.462	1.064
D.M(CCL$_4$)	3.360	1.226	1.204	2.127	2.195	3.144	3.057	2.734	1.669	1.695	2.951	0.869
E_t(W) a.u.	-723.77798	-663.84577	-723.76608	-663.84111	-723.77257	-663.83844	-723.76201	-663.82868	-723.66620	-663.73227	-723.65219	-663.71958
E_t(CCL$_4$)	-723.77284	-663.84023	-723.76108	-663.83574	-723.76746	-663.83272	-723.75581	-663.82401	-723.66300	-663.72832	-723.64626	-663.71577
Charge												
N_3	-0.145	-0.062	-0.117	-0.110	-0.084	-0.023	-0.040	-0.061	-0.084	-0.021	-0.033	-0.054
C_4	-0.420	-0.438	-0.142	-0.560	-0.178	-0.209	-0.185	-0.364	-0.062	-0.121	-0.154	-0.141
C_5	0.073	0.144	-0.036	0.574	-0.309	-0.328	-0.247	0.111	-0.455	-0.367	-0.255	-0.097
N_6	-0.321	-0.324	-0.312	-0.329	-0.286	-0.292	-0.237	-0.281	-0.321	-0.314	-0.260	-0.325
H_7	0.240	0.238	0.247	0.235	0.222	0.229	0.237	0.248	0.280	0.279	0.277	0.314
X_9	-0.113	-0.573	-0.184	-0.739	-0.093	-0.602	-0.065	-0.524	-0.085	-0.578	-0.121	-0.560

Zero point energy **ZPE**, thermal correction **TC** Kcal/mol, and entropy **S** cal/mol-K.

(4) The reactivity of **5CH$_3$-4ATH** is higher than that of the parent **4ATH** and equal to that of **5F-4ATH**, while the reactivity of **2F-4ATH** is the least one according to the (ΔE_g) values.

(ΔE_g) (5.162 eV) **2F-4ATH** > (4.960 eV) **4ATH** > (4.944 eV) **2CH$_3$-4ATH** > (4.906 eV) **5F-4ATH**≈ (4.903 eV) **5CH$_3$-4ATH**.

4.3.3.4. *SOLVENT EFFECT*

The dipole moments of **4ATH** derivatives, in gas and in solutions, are given in Table (38). **2F-4ATH** and **5CH$_3$-4ATH** have higher dipole moment than the other two compounds and the parent. The dipole moment of amino and imino increases as one goes from gas to solutions.

(Dipole Moment (gas)**)** **2F-4ATH** (2.969 D) > **5CH$_3$-4ATH** (1.844 D) > **4ATH** (1.574 D) > **2CH$_3$-4ATH** (1.142 D) > **5F-4ATH** (1.087 D).

The solvents do not affect the equilibrium constant of **2F-4ATH** because the two forms are equally stabilized in both solutions, Table (39). The other compounds are slightly affected by solvents, which reflect on their ΔG°_{soln} values that nearly equal to that in gas phase.

Table (39): The solvation energy G_s°, the free energy of solvation ΔG_s°, the relative free energy in the solvents ΔG_{soln}°, the relative free energy in gas phase ΔG_g°, and the equilibrium constants K_{soln} in water (w) and CCl_4 of 2- and 5-substituted **4ATH** and their tautomers calculated at the **B3LYP / 6-311++G****.

Tautomers	G°_s Kcal/mol	ΔG°_s Kcal/mol	ΔG°_g Kcal/mol	ΔG°_{soln} Kcal/mol	K_{soln}	K_g
2F-4ATH						
(w)	-5.59	0.0				
(CCl_4)	-2.37	0.0				
2F-45ITH			3.44			3.31×10^2
(w)	-5.63	-0.04		3.40	3.10×10^2	
(CCl_4)	-2.42	-0.05		3.39	3.05×10^2	
$2CH_3$-4ATH						
(w)	-5.94	0.0				
(CCl_4)	-2.46	0.0				
$2CH_3$-45ITH			4.01			8.71×10^2
(w)	-6.38	-0.44		3.57	4.14×10^2	
(CCl_4)	-2.79	-0.33		3.68	4.98×10^2	
5F-4ATH						
(w)	-5.53	0.0				
(CCl_4)	-2.39	0.0				
5F-45ITH			4.12			1.04×10^3
(w)	-6.76	-1.23		2.89	1.31×10^2	
(CCl_4)	-2.87	-0.48		3.64	4.66×10^2	
$5CH_3$-4ATH						
(w)	-5.82	0.0				
(CCl_4)	-2.45	0.0				
$5CH_3$-45ITH			8.02			7.51×10^5
(w)	-5.89	-0.07		7.95	6.71×10^5	
(CCl_4)	-2.96	-0.51		7.51	3.19×10^5	

4.4. Thione ⇌ Thiol and keto-enol equilibrium

The equilibrium between the thione and thiol or keto and enol tautomers of five membered rings is particular only interesting. Since it offers the possibility of sulphur or oxygen and nitrogen coordination. For six-membered rings containing one or two nitrogen atoms, the spectral and theoretical data showed that the keto- or thio- forms exist mainly in polar solutions while in non-polar media the equilibrium is displaced to predominance of enol and thiol tautomers(177). In gas phase, the thiol tautomer of 2-thiopyrimidine is more stable while in polar solvents the thione form becomes the more stable one(178).

In this part, hydroxythiazole **2HTH** and its thiol- **2MTH** will be studied at the B3LYP/6-311++G** method and compare the results with their aza analogs (**2ATH**). The effects of type of exohetero atom on tautomeric equilibrium will be investigated. To our knowledge, the literature does not contain a reliable theoretical study on **2HTH** and **2MTH**.

4.4.1. ***GEOMETRY***

Table (40) contains the parameters of the most stable conformers of each tautomer of the three compounds. The results given in this table show the following points:

Fig (6): Structure and numbering system of 2-hydroxythiazole and 2-mercaptothiazole.



X = S	2-MERCAPTOTHIAZOLE	2MTH
	THIAZOLE-2(3H)-THIONE	23TTH
X = O	2-HYDROXYTHIAZOLE	2HTH
	THIAZOLE-2(3H)-ONE	23OTH

Table (40): Geometrical parameters of the three isomers (**2ATH**, **2HTH** and **2MTH**) calculated at **B3LYP / 6-311++G****.

PARAMETER	2ATH	2HTH	2MTH
Bond Length Å			
Bond Order			
S_1C_2	1.767 (1.809)[a] [1.745][b] *0.996 (0.907) [1.072]*	1.751 (1.816)[a] [1.739][b] *1.032 (0.956) [1.128]*	1.759 (1.774)[a] [1.729][b] *0.984 (0.984) [1.096]*
S_1C_5	1 .749 (1.768) [1.780] *1.027 (0.965) [0.973]*	1.749 (1.760) [1.775] *1.032 (0.971) [0.981]*	1.740 (1.755) [1.759] *1.046 (1.000) [1.027]*
C_2N_3	1.298 (1.385) [1.345] *1.758 (1.140) [1.303]*	1.291 (1.381) [1.329] *1.723 (1.104) [1.278]*	1.297 (1.369) [1.333] *1.718 (1.158) [1.339]*
N_3C_4	1.379 (1.385) [1.372] *0.930 (0.863) [1.000]*	1.383 (1.389) [1.379] *0.975 (0.860) [1.014]*	1.378 (1.385) [1.377] *0.971 (0.840) [0.926]*
C_4C_5	1.356 (1.341) [1.356] *1.908 (2.101) [1.976]*	1.357 (1.342) [1.355] *1.952 (2.106) [2.014]*	1.359 (1.345) [1.358] *1.843 (2.025) [1.884]*
C_2X_6	1.377 (1.272) [1.321] *1.163 (1.893) [1.373]*	1.342 (1.206) [1.280] *1.164 (1.878) [1.325]*	1.768 (1.655) [1.723] *0.843 (1.549) [1.020]*
X_6H_7	1.011 (2.571) [1.410] *0.934 --- [0.407]*	0.968 (2.598) [1.372] *0.887 --- [0.410]*	1.348 (2.877) [1.717] *0.984 --- [0.618]*
N_3H_7	2.524 (1.009) [1.326] --- *(0.898) [0.491]*	2.374 (1.010) [1.329] --- *(0.896) [0.462]*	2.605 (1.010) [1.366] --- *(0.888) [0.319]*
Bond Angles			
degree			
$N_3C_2S_1$	114.8 (106.4) [112.2]	116.1 (106.4) [113.2]	124.9 (106.6) [109.1]
$C_4N_3C_2$	110.8 (117.0) [113.9]	110.1 (117.1) [113.8]	110.8 (117.5) [113.9]
$C_5C_4N_3$	116.7 (114.2) [114.1]	116.2 (113.7) [113.4]	116.1 (113.0) [113.5]
$X_6C_2S_1$	121.1 (130.4) [141.3]	118.7 (126.5) [137.1]	120.2 (126.7) [138.6]
$H_7X_6C_2$	113.4 (118.7) [76.6]	107.1 (118.9) [72.9]	93.4 (118.7) [81.5]
Dihedral Angles			
degree			
$N_3C_2S_1X_6$	176.4 (180.0) [-174.6]	180.0 (180.0) [180.0]	180.0 (180.0) [180.0]
$C_4N_3C_2S_1$	0.1 (0.0) [3.2]	0.0 (0.0) [0.0]	0.0 (0.0) [0.0]
$C_5C_4N_3C_2$	0.4 (0.0) [-3.0]	0.0 (0.0) [0.0]	0.0 (0.0) [0.0]
$X_6C_2S_1N_3$	176.4 (180.0) [-174.6]	180.0 (180.0) [180.0]	180.0 (180.0) [180.0]
$H_7N_6C_2N_3$	15.4 (0.0) [1.7]	0.0 (0.0) [0.0]	0.0 (0.0) [0.0]

Values in italic refer to **Bond Order**.

(1) The bonds C_1S, C_5S, C_2N_3 are longer in case of **2ATH** than the other two analogs. The bond C_2N_3 is shorter in **2HTH** (more double) and longer C_4N_3 (more single) than the others. Consequently, the participation of the lone pair of electrons of nitrogen atom N_3 in ring delocalization is higher in case of **2ATH** and is the least in case of **2HTH**.

(2) The order of C_2N_3 bond length in the three tautomers compounds is:

23ITH < 23OTH < 23TTH

(3) The atomic negative charge at N_3 is

(-0.146) **2ATH** > (-0.124) **2HTH** > (-0.015) **2MTH**,

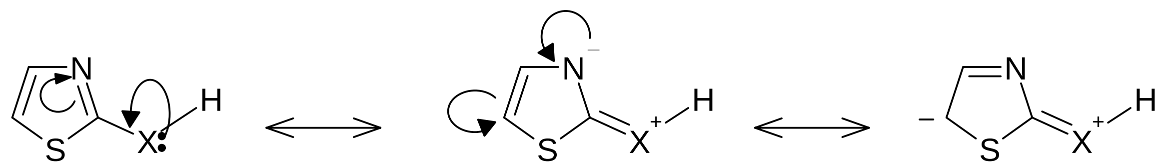
and the order of positive charge at the migrated hydrogen atom H_7 is:

(0.286) **2HTH** > (0.257) **2ATH** > (0.089) **2MTH**

This means that the hydrogen transfer in case of **2HTH** is easier**.**

(4) The magnitude of the gaseous dipole moment is arranged as

(0.648 D) **2HTH** < (1.036 D) **2MTH** < (1.705 D) **2ATH** < (2.728 D) **23ITH** < (4.431 D) **23OTH** < (5.296 D) **23TTH.**



Therefore, these equilibrium reactions have different medium influence as will be seen in next section.

(5) The stability of HOMO of the three compounds increases from **2ATH** (least one) to **2HTH** (highest one). Therefore, the magnitude of IP is

ordered as (5.932 eV) **23TTH** < (6.074 eV) **2ATH** < (6.340 eV) **23OTH** < (6.468 eV) **2MTH** < (6.621 eV) **2HTH**, Table (41).

According to the HOMO-LUMO gap (ΔE_g), the reactivity of **2MTH** is higher than **2ATH**, while **2HTH** has the least reactive one, Table (41). (ΔE_g) (4.522 eV) **2TTH** < (5.301 eV) **2MTH** < (5.445 eV) **2ATH** < (5.771 eV) **23OTH** < (5.881 eV) **2HTH**. The negative charge on C_4 is higher in case of **2ATH** i.e. the electrophilic reactions occur at this position is easier in case of **2ATH**, while the negative charge on C_5 is higher in case of **23OTH** indicating its high tendency for electrophilic.

4.4.2. ***ENERGIES AND RELATIVE STABILITIES***

Tables (41 and 42) present the total energies, relative energies, activation energies, enthalpy of tautomerization, Gibbs free energies, and equilibrium constants for the three processes. The tautomerization **2ATH** $\rightleftharpoons$ **23ITH** is endothermic one with ΔH = 7.23 Kcal/mol and activation energy E_a = 46.64 Kcal/mol. This leads to the conclusion of the predominance of **2ATH** form in gas phase ($K=1.82\times10^5$). The other two processes **2HTH** $\rightleftharpoons$ **23OTH** and **2MTH** $\rightleftharpoons$ **23TTH** are exothermic with ΔH values of -10.82 and -2.89 Kcal/mol, respectively. Their activation energies E_a are 35.46 and 28.58 Kcal/mol, respectively. The tautomerizations shift to the formation of keto and thione forms, as indicated by the Gibbs free energy (negative value) -10.98 and -2.36

Kcal/mol and equilibrium values (Table 41). These findings are in good agreement with the experimental data in literature[31,41,69], where **2ATH**, **23OTH**, and **23TTH** are the predominant species[8,179,180].

4.4.3. ***SOLVENT EFFECT***

The calculated dipole moments in different phases of each tautomer of the studied compounds are given in Table (41). The gaseous dipole moment is the lowest one for each tautomer and it increases in the two solutions where it has its maximum value in water. The increase in dipole moment value on going from gas to solutions is much more pronounced in case of **2MTH** and **2HTH** than **2ATH**. This is reflected on their Gibbs free energy of solvation $\Delta G°_s$ that shows an extra stability for **23OTH** and **23TTH** in both solvents while **2ATH** is the form that stabilizes in the two solvents. Therefore, the relative Gibbs free energy of each of the two forms in solutions shows that the amounts of **23ITH** increase but still the species **2ATH** is the predominant one (Table 43). The corresponding values for the two analogs **23OTH** and **23TTH** in solution show an increase of their amounts more than that in gas phase.

Table (41): Total energy in gas, water (w), and CCl_4, net charges, Ionization Potential **IP**, ΔE_g, dipole moment in gas, water, and CCl_4 of **2ATH**, **2HTH** and **2MTH** calculated at the **B3LYP/6-311++G*.**

Parameter	2ATH	2HTH	2MTH	23ITH	23OTH	23TTH	TS_1	TS_2	TS_3
E_t(gas) a.u.	-624.50691	-644.37795	-967.34097	-624.49454	-644.39538	-967.35251	-624.42032	-644.31170	-967.29040
ZPE	45.02	37.41	33.87	44.76	37.44	36.17	41.06	34.12	32.19
TC	48.42	40.54	37.47	48.15	40.63	39.52	44.41	37.13	35.40
S	74.30	72.76	77.47	74.49	73.30	75.68	74.38	72.34	74.96
E_t(W) a.u.	-624.51708	-644.38592	-967.34725	-624.50592	-644.40842	-967.36515	-624.42593	-644.31903	-967.29603
E_t(CCL_4) a.u.	-624.51124	-644.38144	-967.34364	-624.49940	-644.40104	-967.35787	-624.42265	-644.31487	-967.29280
E_{HOMO} eV	-6.074	-6.621	-6.468	-5.704	-6.340	-5.932			
E_{LUMO} eV	-0.629	-0.740	-1.167	-0.411	-0.569	-1.410			
ΔE_g eV	5.445	5.881	5.301	5.293	5.771	4.522			
IP eV	6.074	6.621	6.468	5.704	6.340	5.932			
Dipole Moment D									
D.M(gas)	1.705	0.648	1.036	2.728	4.431	5.296	1.109	3.094	3.549
D.M(W)	2.293	0.989	1.399	3.678	5.964	7.469	1.461	4.163	4.827
D.M(CCL_4)	1.928	0.783	1.181	3.143	5.079	6.206	1.248	3.550	4.122
Charge									
N_3	-0.146	-0.124	-0.015	-0.069	-0.091	-0.000	-0.146	-0.147	0.076
C_4	-0.295	-0.278	-0.271	-0.204	-0.203	-0.205	-0.316	-0.294	-0.361
C_5	-0.143	-0.170	-0.107	-0.217	-0.232	-0.203	-0.181	-0.197	-0.100
X_6	-0.214	-0.177	-0.011	-0.342	-0.345	-0.279	-0.430	-0.346	-0.209
H_7	0.257	0.286	0.089	0.317	0.320	0.329	0.337	0.334	0.155

Zero point nergy **ZPE**, thermal correction **TC** Kcal/mol, and entropy **S** cal/mol-K

Table (42): Relative stabilities conversion barrier **ΔE***(kcal/mol), activation energy $\mathbf{E_a}$(kcal/mol), reaction enthalpy **ΔH** (kcal/mol), and Gibbs free energy **ΔG** (Kcal/mol), and equilibrium constant **K** of **2ATH**, **2HTH** and **2MTH** calculated at the **B3LYP / 6-311++G**.**

	2ATH=23ITH	**2HTH=23OTH**	**2MTH=23TTH**
ΔE*	54.34	41.57	31.73
Ea	46.64	35.46	28.58
ΔE	7.76	-10.94	-7.24
ΔH	7.23	-10.82	-2.89
ΔG	7.18	-10.98	-2.36
LogK	-5.2593	8.0465	1.7280
K	1.82×10^{5}	8.98×10^{-9}	1.87×10^{-2}

Table (43): The solvation energy G°_{s}, the free energy of solvation ΔG°_{s}, the relative free energy in the solvents ΔG°_{soln}, the relative free energy in gas phase ΔG°_{g}, the equilibrium constants K_{soln} in water (w) and CCl_4 and the equilibrium constants $\mathbf{K_g}$ in gas phase of **2ATH**, **2HTH**, **2MTH** and their tautomers calculated at the **B3LYP / 6-311++G****.

Tautomers	G°_{s} Kcal/mol	ΔG°_{s} Kcal/mol	ΔG°_{g} Kcal/mol	ΔG°_{soln} Kcal/mol	K_{soln}	K_g
2ATH						
(w)	-6.38	0.0				
(CCl_4)	-2.72	0.0				
23ITH			7.18			1.82×10^{5}
(w)	-7.14	-0.76		6.42	5.08×10^{4}	
(CCl_4)	-3.05	-0.33		6.85	1.05×10^{5}	
2HTH						
(w)	-5.00	0.0				
(CCl_4)	-2.19	0.0				
23OTH			-10.98			8.98×10^{-9}
(w)	-8.18	-3.18		-14.16	4.18×10^{-11}	
(CCl_4)	-3.55	-1.36		-12.34	9.02×10^{-10}	
2MTH						
(w)	-3.94	0.0				
(CCl_4)	-1.68	0.0				
23TTH			-2.36			1.87×10^{-2}
(w)	-7.93	-3.99		-6.35	2.22×10^{-5}	
(CCl_4)	-3.36	-1.68		-4.04	1.09×10^{-3}	

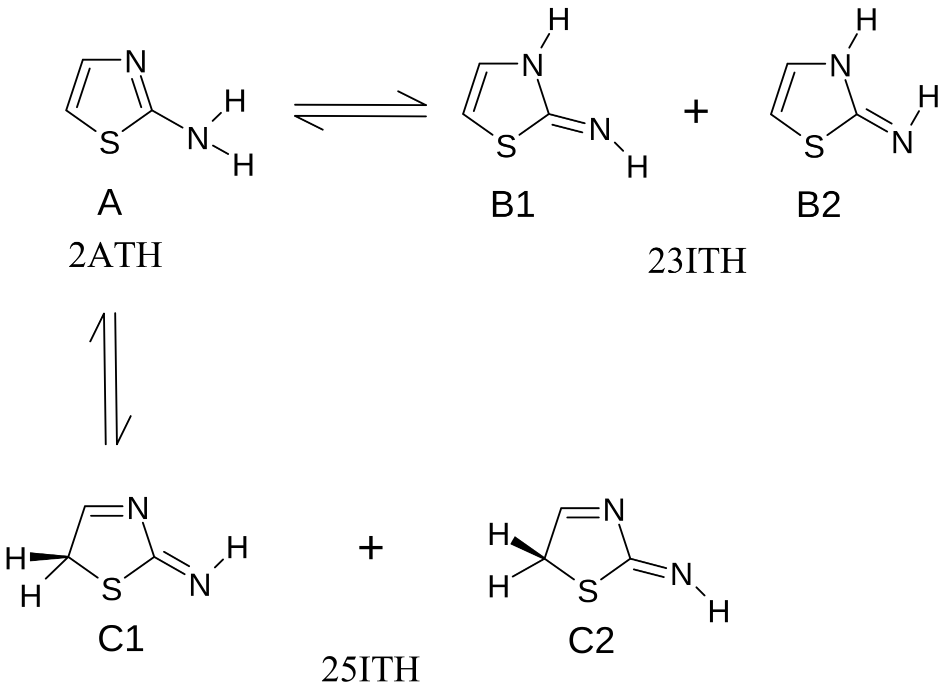
SUMMARY

SUMMARY

Molecular orbital calculations were performed on 2- and 4-X thiazole derivatives, where X=NH_2, OH or SH, at B3LYP and MP2 methods in order to study the 1,3-hydrogen transfer between X group and endocyclic nitrogen atom or carbon atom at position five.

1. 2-AMINOTHIAZOLE

The calculations show that 2-aminothiazole **2ATH** is a planar compound but the exocyclic N-atom is slightly out of the thiazole ring plane. The values of the bond lengths of the thiazole ring are not of pure single or double bonds indicating its aromaticity character. The HF method fails to describe well the aromaticity of this system, while in case of MP2 and B3LYP methods increasing the basis set size by additional higher momentum angular orbitals was sufficient for very accurate estimation of the ground state properties of our system. Comparing to the geometry of **2ATH** molecule the two imino forms [B, C] are also planar, with geometry totally different from the corresponding amino tautomer, due to disappearance of ring aromaticity. The change in bond length and angels attributed to the difference in extent of nitrogen lone pair in conjugation in the different isomers.



The exocyclic nitrogen atom (N_6) has negative charge, which is higher than that on endocyclic atom (N_3) in all levels. While the atomic charge on C_5 is less than that on C_4. This means that **2ATH** is a polar molecule, which seems to be dominated by the lone pairs of exo- and endocyclic nitrogen atoms with little perturbing effect of the sulfur lone pair.

2. 4- AND 5-AMINOTHIAZOLES

The position of $-NH_2$ group does not appreciably affect the E_{HOMO} and E_{LUMO} of amino thiazoles, **2ATH** and **5ATH** have nearly the same IP (8.536 and 8.525 eV) and IP of **4ATH** is 8.370 eV. On the other hand, E_{LUMO} of **2ATH** and **4ATH** is 1.113 and 1.105 eV while that for **5ATH** is 0.982 eV. The order of IP of all aminothiazoles tautomers is (MP2 results)

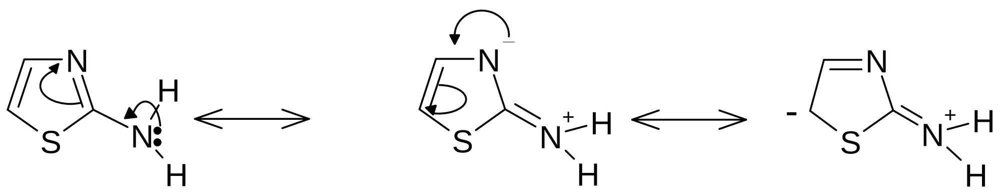
23ITH < 4ATH < 5ATH ≈ 2ATH < 45ITH ≈ 25ITH < 54ITH.

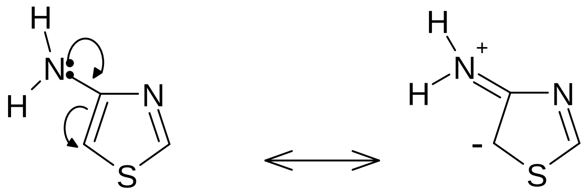
The order of the energy gap (ΔE_g) which is considered as a measure of the reactivity of the compound is as follows (MP2 results) **23ITH** (8.986 eV) < **4ATH** (9.475 eV) < **5ATH** (9.510 eV) < **2ATH** (9.649 eV) < **25ITH** (10.474 eV) < **45ITH** (10.694 eV) < **54ITH** (10.857 eV) which means that **2ATH** is less reactive than both of **4ATH** and **5ATH** isomers while the least reactive one is the imino **54ITH**.

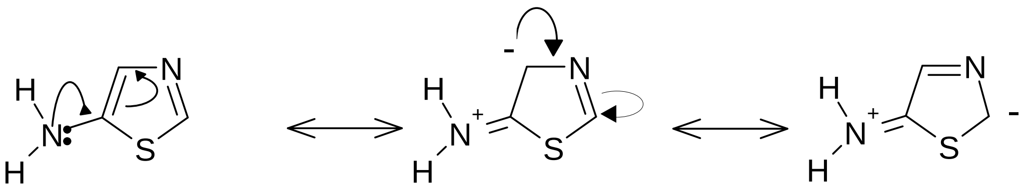
2ATH form is found to be the most stable one at all levels of calculations while the least one is **25ITH,** i.e. the order of stability is

2ATH > 23ITH >25ITH

The addition of both (ZPE) and (TC) does not affect the order of their relative stabilities. The Gibbs free energy change ΔG of the process is calculated at the three levels and give the values 8.06, 7.18 and 10.59 Kcal/mol. These values are very similar to the corresponding relative stability values of enthalpy term ΔH, due to small effect of entropy contribution. On the other hand, the total energy of the isomer 4-aminothiazole **4ATH** is higher than that of the corresponding 2-isomer **2ATH** by 2.08, 1.29 Kcal/mol at the B3LYP and MP2 levels of calculations, while the least stable aminothiazole is **5ATH**. This is can be explained in terms of their resonance contributions.







Comparing between the results of the three aminothiazoles isomers **2ATH**, **4ATH** and **5ATH**, one can notice that:

(1) In the three isomers, the amino form is the predominant form as indicated by the values of ΔG and K_T parameters.

(2) The tautomerization activating energy of **2ATH** $\rightleftharpoons$ **23ITH** is lower than that of **4ATH** and **5ATH** where the difference is around 17.35 and 20.05 Kcal/mol, respectively calculated at the B3LYP level.

(3) The enthalpy value (ΔH) for the two isomers **2ATH** and **4ATH** are comparable ≈7.3 Kcal/mol. The same trend is found also for the free energy change ΔG.

(4) The IP of **2ATH** and **5ATH** is higher than that of **4ATH**, while the electron affinity of **2ATH** and **4ATH** are nearly equal and is greater than of **5ATH**.

The results show that all species are more stabilized with different extents in both media but the stabilization energy in water is greater. For aminothiazoles, one notices that in spite of the solvent stability of imino form is greater than its amino, the latter still the predominant species in solution and thus the same stability trends of the tautomers as in the case of the gaseous phase are found:

2ATH > 3ITH > 5ITH

4ATH > 45ITH

5ATH > 54ITH

3. DIAMINOTHIAZOLES

The calculations performed on diaminothiazole indicate that the presence of two amino groups that remarkably affect the two C-S bonds and C_5-C_4 bond. The C-S bond elongates by 0.02Å comparing to **4ATH** but shortens by 0.01Å with respect to **2ATH** while C_5-C_4 bond decreases by 0.007Å and elongates by 0.01Å with respect to **4ATH**. The differences in bond length between the imino forms (**2A5ITH**, **3I4ATH** and **5I4ATH**) comparing to the corresponding mono imino compounds (**4ITH**, **3ITH** and **5ITH**) is attributed to the extent of involvement of N_3 lone pair in resonance. The first group has more conjugation, **25ATH** has longer C_2S_1, C_5S_1, C_4C_5 and C_2N_6 bonds than **2ATH** or **24ATH** while C_2N_3 is shorter. This means that 5-NH_2 group decreases the extent of delocalization over

the thiazole ring. The same trends were found in case of 5-aminothiazole-2(3H)-imino **3I5ATH** comparing to **3I4ATH** isomers.

The gas phase dipole moment values of the five tautomers of 2,4-diaminothiazole vary from 0.566 D to 6.633 D at B3LYP level, and can be arranged as follows: **24ATH < 3I5ITH < 3I4ATH < 2A5ITH < 5I4ATH.** This is can be attributed to the directions of the dipole vectors of the two amino or imino groups. The order of their IP calculated at MP2 level is

3I4ATH ≈ 24ATH < 5I4ATH ≈ 2A5ITH < 3I5ITH.

Consequently, the order of mono and diaminothiazoles energy gap ΔE_g is; **2ATH** (9.649 eV) > **4ATH** (9.475 eV) > **24ATH** (9.007 eV) i.e. the reactivity of the diamino is higher than the reactivities of both monoaminothiazoles. The reactivity of the five tautomers of 2,4-diaminothiazole has the arrangement **3I4ATH > 24ATH > 5I4ATH > 2A5ITH > 3I5ITH.**

The B3LYP/6-311++G** calculations of their relative stabilities show that the most stable one in gas phase is **2A5ITH** i.e. local minimum, while **3I4ATH** is the highest one in energy. The order of stability of the five structures is; **2A5ITH > 24ATH ≈ 5I4ATH > 3I5ITH > 3I4ATH**. In case of MP2 results, their stability order becomes **24ATH > 2A5ITH > 5I4ATH > 3I5ITH > 3I4ATH**. Comparing to the results for monoaminothiazoles (**2ATH** and **4ATH**) one can notice that,

(1) The amino substitution in 4-position in case of **2ATH** destabilizes the imino form, i.e. the process **24ATH** $\rightleftharpoons$ **3I4ATH** becomes more endothermic. Consequently, the free energy change ΔG has more positive value.

(2) For **4ATH** tautomerization, the introduction of the substituent $-NH_2$ group in position two facilitates the hydrogen transfer **24ATH** $\rightleftharpoons$ **2A5ITH** and the reaction enthalpy becomes (-0.84 Kcal/mol) with a decrease of activation energy E_a (55.62 Kcal/mol).

(3) The existence of $-NH_2$ group in position (four) also increases the stability and the percent of the imino **5I4ATH** to reach (0.56) instead of (1.12×10^8) in case of **5ITH**.

(4) The diimino structure **3I5ITH** has only energy 2.23 Kcal/mol more than the diamino one (**24ATH**).

4. SUBSTITUTED-AMINOTHIAZOLES

The effect of type of substituent and position on the studied equilibrium is study at the same levels. Methyl group (electron donating) in position four increases only the bond length (C_4-N_3) in both forms, while electron accepting (withdrawing) groups (F, Cl) shorten the C_4-N_3 bond length in the two forms. The substituents NO_2 and CHO disturb the geometry of thiazole cycle due to their participating in ring delocalization and certain interactions between the negatively charge carbonyl or nitro

oxygen with hydrogen C_5, C_5H (O...H=2.62 Å). The substituent effect in position five on **2ATH** and **23ITH** geometry is more pronounced than that in position four in case of electron withdrawing ones while 5-CH_3 group elongates only S-C_5 bond. The endocyclic nitrogen atom charge is more influenced by 4-substituents than by 5-substitution.

The energy gap ΔE_g has its maximum value for –NO_2 substituent, while that of –Cl derivative is nearly equal to that of the parent **2ATH**.

(1) The substituent position does not affect values or trend of IP or E_{HOMO}, while E_{LUMO} values have the same trend of 4-position except of –Cl, and –F.

(2) ΔE_g of **2ATH** is higher than that of 5-CH_3 derivative and equal to that 5-Cl one at MP2 level, while the other three electron withdrawing groups have higher values. According to that, the reactivity of **5-CH_3-2ATH** is higher than **2ATH** and the other derivatives. The charges on C_5 and C_4 in case of **5-CH_3-2ATH** indicate its higher reactivity for nucleophilic and electrophilic substitutions, respectively.

The effect of substituent on the relative stabilities and thermodynamics can be summarized as

(1) 4-Me, 4-F and 4-Cl isomers are more stable than their 5-isomers while the reverse is found in case of nitro and formyl isomers due to their participation in the ring delocalization in 5-position.

(2) In all cases, the amino form is more stable than its imino form leading to endothermic enthalpy, as in case of the unsubstituted **2ATH**, i.e. the type and position of ring substituent do not affect the relative stability of amino and imino tautomers.

The relative Gibbs free energy of 4-isomers in both solutions become higher than that in gas phase, that's due to the more stabilization of amino form over its imino in the two solutions, except in case of 4-CHO and 4-CH_3.

The 5-derivative imino tautomers are more solvated than their amino forms, which explains the decrease of their relative Gibbs free energy in solutions than in gas phase. Yet, this does not affect the relative stability of amino and imino forms and therefore, the amino form is still the main tautomer in both solutions. The only change is the decrease of equilibrium constant K value comparing to its value in gas phase.

The presence of a nitro group (strong electron withdrawing group) attached to the exocyclic nitrogen slightly elongates the C_2N_3 bond and shortens the two CS bonds comparing to the **2ATH** itself. This means that an increase in extent of conjugation of lone pair of exocyclic nitrogen with the thiazole ring occurs. In addition, the acidity of exocyclic –NH_2 increases, the positive charge of hydrogen atom is 0.326 i.e. it increases by 0.07 more than that in case of unsubstituted **2ATH**, which facilitates its transfer to the endocyclic nitrogen atom N_3. ΔE_g which is less by 0.92 eV than that of

2ATH i.e. it is more reactive. In addition, the presence of NO_2 group duplicates the dipole moment of amino tautomer and increases that of its imino form by three times. The imino **NNO_2-23ITH** total energy is less than **NNO_2-2ATH** by only 0.00065 a.u. (0.41 Kcal/mol) i.e. in gas phase the imino is more stable by only 0.41 Kcal/mol. The data also shows a decrease in reaction activation energy E_a by 6.65 Kcal/mol comparing to **2ATH**. Consequently, the process becomes easier, leading to the coexist of two forms in the gas phase. The Gibbs free energy in both solutions are -6.22 and -2.61 Kcal/mol i.e. the tautomerization becomes spontaneous in solutions at room temperature. The equilibrium constants are 2.76×10^{-5} and 1.22×10^{-2} in H_2O and CCl_4, respectively. In solution, **NNO_2-23ITH** is more predominate.

The electron with drawing group (-F) in position two elongates the two single bonds C_4N_3 and C_5S_1, while C_4N_6 bond shortens by 0.003Å. This lead to less participation of exocyclic nitrogen lone pair into delocalization of the ring. On other hand, the $–CH_3$ group affects only CS bond (elongate). The substitution of **4ATH** in position five has little effect in its geometry comparing to that in position two.

The values of ΔG and K of such derivatives indicate an increase of the imino form concentration more than in case of **4ATH**, except for **$5CH_3$-4ATH** derivative. The solvent has not effect on the relative stability or equilibrium constant for these derivatives.

5. Thione $\rightleftharpoons$ Thiol and keto-enol equilibrium

2-hydroxy and 2-mercaptothiazole exist mainly in the keto- and thio- forms. The differences in energy are -10.94 and -7.24 Kcal/mol, respectively. The Gibbs free energy in gas phase are -10.98 and -2.36 Kcal/mol, respectively, while the equilibrium constants are 8.98×10^{-9} and 1.87×10^{-2}, respectively. The dipole moments are (0.648 D) **2HTH** < (1.036 D) **2MTH <** (4.431 D) **23OTH <** (5.296 D) **23TTH.** In solution, the two forms (keto- and thiothiazoles) still more predominant.

ARABIC SUMMARY

الملخص العربي

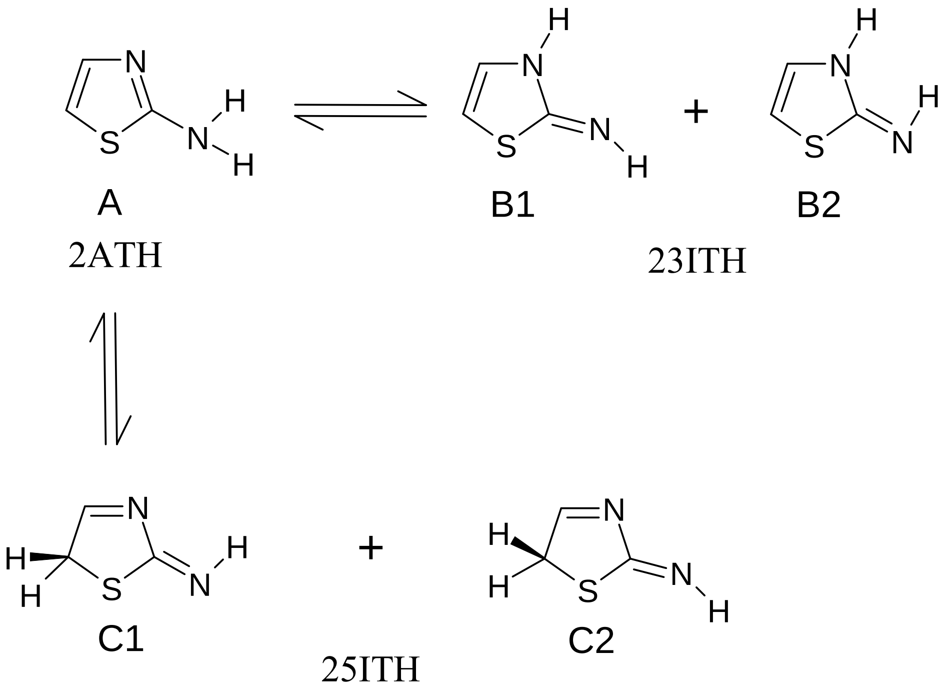
لقد استخدمت طريقة حسابات المدارات الجزيئية على مشتقات (2- and 4-X) ثيازول حيث (X=NH_2, OH or SH) بإستخدام نظرية مولر- بلست (MP2) ونظرية كثافة الدالة (DFT) لدراسة الإنتقال (٣،١) لذرة الهيدروجين من المجموعة (X) إلى ذرة النيتروجين الموجودة في حلقة الثيازول أو الى ذرة الكربون في الموضع (٥).

١) ٢-أمينوثيازول

لقد أوضحت الحسابات أن مركب ٢-أمينوثيازول هو مركب مستوى و أن ذرة النيتروجين في حلقة الثيازول ليست في مستوى الحلقة، كما أن أطوال الروابط في حلقة الثيازول ليست أحادية أو ثنائية تماماً مما يدل على الخاصية الأروماتية للمركب.

عجزت نظرية هارتري- فوك (HF) عن شرح الخاصية الأروماتية لهذا النظام بينما في حالة إستخدام نظريتي (B3LYP and MP2) مع الزيادة في حجم قاعدة المجموعة بإضافة (higher momentum angular orbital) نجحت في تعيين خواص الحالة المستقرة بدقة لهذا النظام.

بمقارنة الشكل الهندسي لمركبي الإيمينو [B,C] مع ٢-أمينوثيازول نجد أن لها الشكل المستوى أيضاً ولكنهما يختلفان تماماً عن متشكل الأمينو نتيجة لإختفاء الخاصية الأروماتية لحلقة الثيازول كما أن الإختلاف في أطوال الروابط و الزوايا هو نتيجة لإختلاف الإقتران لـ (lone pair) لذرة النيتروجين في المتشكلات المختلفة.



جميع النظريات أثبتت أن ذرة النيتروجين N_6 خارج حلقة الثيازول تحمل شحنة سالبه أعلى من ذرة النيتروجين N_3 داخل حلقة الثيازول، وأن الشحنة الذرية على ذرة الكربون C_5 أقل من الشحنة على ذرة الكربون C_4 مما يدل على أن المركب ٢-أمينوثيازول هو مركب قطبي وهو الأكثر ثباتاً نتيجة لـ (lone pairs) لذرتي النيتروجين داخل وخارج حلقة الثيازول بينما (lone pair) لذرة الكبريت فهو قليل التأثير على المركب.

٢) ٤-أمينوثيازول و ٥-أمينوثيازول

إن موضع مجموعة الأمينو ($-NH_2$) لا يؤثر تأثير واضح على قيم E_{HOMO} , E_{LUMO} لمركب الأمينوثيازول، فنجد أن ٢-أمينوثيازول و ٥-أمينوثيازول لهما قيمة جهد التأين (IP) متساوية تقريباً (8.536 and 8.525 eV) بينما في ٤-أمينوثيازول فقيمة جهد التأين = eV ٨,٥٢٥ ، كما أن قيمة E_{LUMO} في ٢-أمينوثيازول و ٤-أمينوثيازول = (eV ١,١٠٥ and ١,١١٣) بينما للـ٥-أمينوثيازول = eV ٠,٩٨٢ ، ونجد أن قيمة جهد التأين لجميع متشكلات الأمينوثيازول يمكن ترتيبها كالآتي:

23ITH < 4ATH <5ATH ≈ 2ATH < 45ITH ≈ 25ITH < 54ITH

بينما ترتيب قيم الطاقة ΔE_g للمتشكلات، والتي تعتبر مقياسا لنشاط المركبات يكون كالتالي طبقا لنظرية مولر – وبلست:

23ITH (8.986 eV) **< 4ATH** (9.475 eV) **< 5ATH** (9.510 eV) **< 2ATH** (9.649 eV) **< 25ITH** (10.474 eV) **< 45ITH** (10.694 eV) **< 54ITH** (10.857 eV).

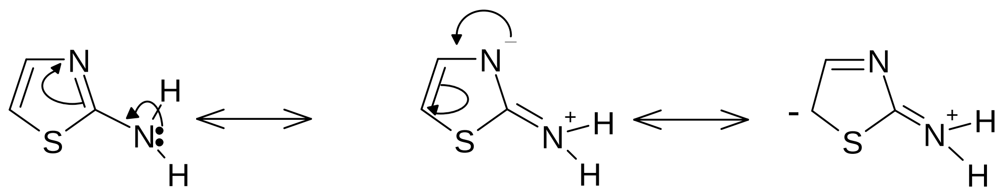
مما يدل على أن ٢-أمينوثيازول هو أقل نشاطا من ٤-أمينوثيازول و ٥-أمينوثيازول بينما الإيمينو **54ITH** هوالأقل نشاطا . المتشكل ٢-أمينوثيازول هو المتشكل الأكثر ثباتا باستخدام جميع النظريات والحسابات بينما الأقل ثباتا هو الايمينو **٢5ITH.**

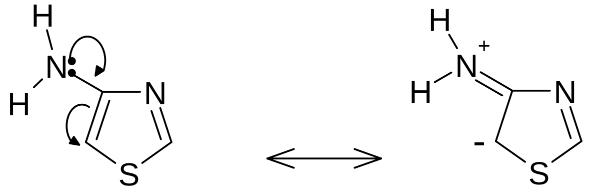
يمكن توضيح استقرار المركبات كالتالي:

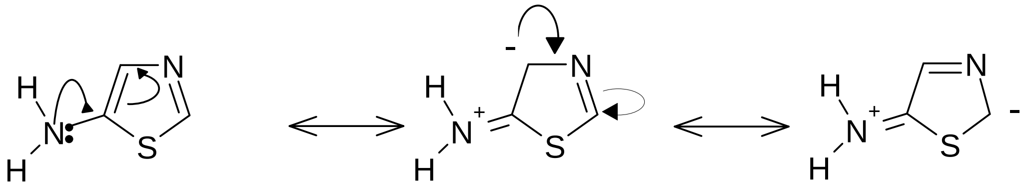
2ATH > ٢3ITH > ٢5ITH

إن إضافة قيم (TC) وطاقة نقطة الصفر (ZPE) ، لا تؤثر على الثبات النسبي للمركبات بينما قيمة التغير في الطاقة الحرة لجبس (ΔG) للعملية تم حسابها بجميع النظريات ولها القيم التالية (٨,٠٦ ،٧,١٨ and ١٠,٥٩ Kcal/mol) وهذه القيم قريبة جدا من المحتوى الحراري (ΔH) وذلك بسبب التأثير الضئيل لمساهمة الإنتروبي S. ومن ناحية أخرى، نجد أن الطاقة الكلية للمتشكل ٤-أمينوثيازول أعلى من طاقة المتشكل ٢-أمينوثيازول بمقدار

(٢,٠٨ Kcal/mol at B3LYP) و (1.29 Kcal/mol at MP2) بينما ٥-أمينوثيازول هو المركب الأقل ثباتا، وهذا يمكن توضيحه من خلال إسهام جميع المتشكلات في عملية الرنين:







بالمقارنة بين متشكلات الأمينوثيازول الثلاثة (٢-أمينوثيازول و٤-أمينوثيازول و٥-أمينوثيازول) يمكن توضيح مايلي:

١) قيم الطاقة الحرة لجبس (ΔG) و ثابت الإتزان K_T يشيران إلى أن المتشكل ٢-أمينوثيازول هو الأكثر ثباتا بين المتشكلات الثلاث.

٢) طاقة التنشيط (ΔE) لعملية التشكل **23ITH** $\rightleftharpoons$ **2ATH** هي أقل من طاقة التنشيط في ٤-أمينوثيازول و ٥-أمينوثيازول بحوالي (١٧,٣٥ and 20.05 Kcal/mol) تقريبا بإستخدام نظرية B3LYP.

٣) قيم المحتوى الحراري (ΔH) للمتشكلين ٢-أمينوثيازول و ٤-أمينوثيازول متقاربتين (7.3 Kcal/mol) ، وكذلك أيضا بالنسبة لقيمة الطاقة الحرة لجبس (ΔG).

٤) قيمة جهد التأين (IP) لـ٢-أمينوثيازول و٥-أمينوثيازول أعلى من قيمة جهد التأين لـ٤-أمينوثيازول، بينما القابلية الالكترونية لـ٢-أمينوثيازول و ٤-أمينوثيازول متقاربتين تقريبا و أعلى من قيمة القابلية الالكترونية لـ٥-أمينوثيازول.

أوضحت النتائج أن جميع المتشكلات تزيد من ثباتها في كلا الوسطين (المحلولين)، وان قيمة طاقة الإستقرار في الماء تكون أكبر.

بالنسبة للأمينوثيازول فبالرغم من أن (solvent stability) للمتشكل الأيمينو أكبرمن الأمينو ، ولكن يظل الأمينو هو المتشكل السائد في المحلول كما هو في الوسط الغازي.

2ATH > 23ITH > 25ITH

4ATH > 45ITH

5ATH > 54ITH

٣) ثنائي الأمينوثيازول

لقد أوضحت الحسابات التي أجريت على ثنائي أمينوثيازول بأن موضع مجموعتي الأمينو له تأثير واضح على الرابطتين S-C و C_4-C_5 في حلقة الثيازول، فنجد ان الرابطة S-C تطول بـ Å ٠,٠٢ مقارنة بالمتشكل ٤-أمينوثيازول بينما تقل بحوالي Å ٠,٠١ بالنسبة لـ٢-أمينوثيازول ، أما الرابطة C_4-C_5 تقل بحوالي Å 0.007 بالنسبة لـ٢-أمينوثيازول و تطول بحوالي Å ٠,٠١ مقارنة بـ٤-أمينوثيازول.

بالمقارنة بين أطوال الروابط في متشكلات الإيمينو في ثنائي الأيمينوثيازول **2A5ITH,** (**3I4ATH** and **5I4ATH**) و متشكلات الإيمينوالمقابلة في الأمينوثيازول **4ITH, 3ITH** and **5ITH** نلاحظ الزيادة في إسهام (lone pair) لذرة النيتروجين N٣ داخل حلقة الثيازول في عملية الرنين. مجموعة الأمينوالأولى يكون فيها عملية الاقتران أكبر، وفي المتشكل **25ATH** تكون الروابط (C_2S_1, C_5S_1, C_4C_5 and C_2N_6) أطول من الروابط المقابلة لها في ٢-أمينوثيازول و ٢،٤-ثنائي أمينوثيازول بينما تكون الرابطة C_2N_3 أقصر، مما يدل على أن المجموعة ($5\text{-}NH_2$) تقلل من (delocalization over the thiazole ring). ونلاحظ الظاهرة نفسها في حالة المتشكل **3I5ATH** بالمقارنة مع المتشكل **3I4ATH**.

قيم العزم ثنائي القطب في الوسط الغازي للمتشكلات الخمسة في٢،٤-ثنائي أمينوثيازول تتراوح مابين 0.566 D إلى 6.633 D باستخدام (B3LYP) ويمكن ترتيبه كالآتي:

24ATH < 3I5ITH < 3I4ATH < 2A5ITH < 5I4ATH

وهذا ينسب إلى اتجاه (dipole vector) لكلا من مجموعتي الأمينو والإيمينو. يمكن ترتيب قيمة جهد التأين لهذه المتشكلات طبقا لنظرية مولر – وبلست كالتالي:

3I4ATH ≈ 24ATH < 5I4ATH ≈ 2A5ITH < 3I5ITH.

ترتيب الطاقة (The energy gap ΔE_g) في ثنائي أمينوثيازول و آحادي أمينوثيازول كالتالي **2ATH** (9.649 eV) > **4ATH** (9.475 eV) > **24ATH** (9.007 eV) وبالتالي فأن نشاط ثنائي الأمينو أكبر من نشاطية كلا متشكلين أحادي أمينوثيازول ، ويمكن ترتيب النشاطية لمتشكلات ثنائي أمينوثيازول الخمسة كالتالي:

3I4ATH > 24ATH > 5I4ATH > 2A5ITH > 3I5ITH

إن حساب الثبات النسبي باستخدام (B3LYP/ 6-311++G**) يوضح أن المتشكل الأكثر ثباتا في الوسط الغازي هو الايمينو **2A5ITH** (قيمة صغرى محلية)، بينما الايمينو **3I4ATH** هو الأعلى في الطاقة. ثبات المتشكلات الخمسة للثنائي أمينوثيازول يمكن ترتيبه كالتالي:

2A5ITH > 24ATH ≈ 5I4ATH > 3I5ITH > 3I4ATH (B3LYP)

24ATH > 2A5ITH > 5I4ATH > 3I5ITH > 3I4ATH (MP2)

بالمقارنة بين النتائج في متشكلي أحادي أمينوثيازول (**2ATH** and **4ATH**) يمكن توضيح ما يلي:

١) مشتق الأمينو في الموضع(٤) في حالة ٢-أمينوثيازول يقلل من استقرارية متشكل الإيمينو مما يدل على أن عملية التشكل **3I4ATH** $\rightleftharpoons$ **24ATH** تصبح ماصة للحرارة أكثر، وبالتالي فان قيمة التغير في الطاقة الحرة لجبس (ΔG) تكون أكثر ايجابية.

٢) بالنسبة لعملية التشكل في ٤-أمينوثيازول فإن إدخال المشتق ($-NH_2$) في الموضع (٢) يعيق انتقال الهيدروجين **2A5ITH** $\rightleftharpoons$ **24ATH** و المحتوى الحراري (ΔH) يصبح (-٠,٨٤ Kcal/mol) مع النقص في قيمة طاقة التنشيط (E_a 55.62 Kcal/mol).

٣) إحلال مجموعة NH_2- في الموضع (٤) يزيد من الثباتية و نسبة تكون الإيمينو **5I4ATH** لتصل إلى (0.56) بالمقابل إلى (1.12×10^8) في حالة **5ITH.**

٤) المتشكل ثنائي الإيمينو **3I5ITH** أعلى في الطاقة من ثنائي الأمينو **24ATH** بمقدار (٢,٢٣ Kcal/mol) .

٤) مشتقات الأمينوثيازول

لقد تم دراسة تأثير نوع و موضع المشتق على موضع الاتزان باستخدام نفس النظريات. مجموعة الميثيل (مجموعة مانحة للالكترونات) في الموضع (٤) تزيد من طول الرابطة C_4-N_3 في كلا المتشكلين (الأمينو والايمينو)، بينما المجاميع الساحبة للالكترونات (F, Cl) تقلل من طول الرابطة C_4-N_3 في كلا المتشكلين. المجاميع NO_2, CHO تعيق الشكل الهندسي لحلقة الثيازول نتيجة لاشتراكها في (ring delocalization) و تفاعلات معينة بين الأوكسجين سالبة الشحنة في مجموعة الكربونيل أوالنيترو مع الهيدروجين المتصلة بالكربون في الموضع (٥) C_5H (O…H 2.62Å) .

تأثير المشتق في الموضع (٥) على الشكل الهندسي لـ٢-أمينوثيازول والايمينو **23ITH** أكثر وضوحا من المشتق في الموضع (٤) في حالة المشتقات الساحبة للالكترونات، بينما المجموعة ($5CH_3$) تطيل فقط الرابطة S-C_5. شحنة ذرة النيتروجين داخل حلقة الثيازول (N_3) تتأثر بشكل أكبر بالمشتق في الموضع (4) .

قيمة الطاقة (The energy gap ΔE_g) له أعلى قيمة في حالة المشتق ($-NO_2$) بينما في حالة المشتق (-Cl) تكون تقريبا مساوية لقيمتها في المتشكل ٢-أمينوثيازول.

١) موضع المشتق لا يؤثر على قيم واتجاة جهد التأين وE_{HOMO} بينما قيم E_{LUMO} لها نفس الاتجاه بالنسبة للمشتقات في الموضع (٤) ما عدا المشتق (F– –Cl and).

٢) الطاقة (ΔE_g) في ٢-أمينوثيازول أعلى من المشتق ($5\text{-}CH_3$) وتكون مساوية للطاقة في المشتق (5Cl)، بينما الثلاث مجاميع الساحبة للإلكترون الأخرى لها قيم عالية، وطبقا لذلك فان النشاطية للمركب $5\text{-}CH_3\text{-}2ATH$ أعلى من المركب ٢-أمينوثيازول ومن مشتقاته الأخرى . الشحنة الموجودة على C_5 و C_4 في المركب **$5\text{-}CH_3\text{-}2ATH$** تشير إلى النشاطية العالية للاستبدال الالكتروفيلي والنيوكليوفيلي على التوالي.

تأثير المشتقات على الثبات النسبي و قيم الثيرموديناميك يمكن تلخيصها كالتالي:

١) المتشكلات $4\text{-}Cl, 4\text{-}F$ and $4\text{-}CH_3$ أكثر ثباتا من المشتقات المقابلة لها في الموضع (٥) ونجد العكس في حالة متشكلات مشتقات النيترو و الألدهيد وذلك بسبب إسهامها في (The ring delocalization) في الموضع (٥).

٢) في جميع الحالات فان مركب الامينو هو الأكثر ثباتا مع تحول ماص للحرارة كما في حالة مركب ٢-أمينوثيازول حيث إن نوع وموضع المشتق في حلقة الثيازول لايؤثر على قيم الثبات النسبي للمتشكلين الأمينو والايمينو.

طاقة جبس الحرة النسبية للمتشكل (٤) في كلا المحلولين تكون أكبر من قيمتها في الوسط الغازي وذلك بسبب زيادة ثبات متشكل الأمينو على متشكل الايمينو في كلا المحلولين ماعدا في حالة المشتقات 4-CHO و $4\text{-}CH_3$. المشتق في الموضع (٥) للمتشكل الايمينو يذوب أكثر من متشكل الامينو وهذا يوضح النقص في قيمة طاقة جبس الحرة النسبية (The relative Gibbs free energy) لها في المحاليل عنها في الوسط الغازي، ولكن ذلك لايؤثر على الثبات النسبي لكلا من المتشكلين (الأمينو و الايمينو)، ولذلك فان هيئة الامينو تظل هي السائدة في كلا المحلولين، والتغير الوحيد الذي يحدث هو النقص في ثابت الاتزان (K) مقارنة بقيمته في الوسط الغازي.

إن وجود مجموعة NO_2 (مجموعة قوية ساحبة للالكترونات) متصلة بذرة النيتروجين خارج حلقة الثيازول يزيد من طول الرابطة C_2N_3 ويقلل من طول الرابطتين CS مقارنة بالمتشكل ٢-أمينوثيازول. مما يدل على حدوث الزيادة في (Conjugation of lone pair) لذرة النيتروجين (N_6) مع حلقة الثيازول، بالإضافة إلى ذلك فان حامضية مجموعة NH_2- الخارجية تزداد، حيث أن الشحنة الموجبة لذرة الهيدروجين = ٠,٣٢٦ مما يعني إنها زادت بحوالي ٠,٠٧ عن متشكل ٢-أمينوثيازول مما يسهل انتقالها إلى ذرة النيتروجين (N_3) داخل حلقة الثيازول. قيمة الطاقة (ΔE_g) تقل بمقدار ٠,٩٢ eV عن قيمتها في المتشكل ٢-أمينوثيازول مما يدل على انه أكثر نشاطية. إن وجود مجموعة NO_2 تضاعف قيمة العزم ثنائي القطب لمتشكل الأمينو كما إنها تزيد من قيمتها في متشكل الايمينو إلى ثلاثة أضعاف.

متشكل الايمينو **NNO$_2$-23ITH** اقل في الطاقة من متشكل الأمينو **NNO$_2$-2ATH** بحوالي ٠,٠٠٠٦٥ a.u. (0.4 Kcal/mol) في الوسط الغازي مما يدل على أن متشكل الايمينو أكثر ثباتا في الوسط الغازي بحوالي (0.4 Kcal/mol).

النتائج أوضحت نقص في قيمة (E_a) طاقة تنشيط التفاعل بمقدار 6.65 Kcal/mol مقارنة بـ٢-أمينوثيازول وبالتالي فان العملية تكون أكثر سهولة مما يؤدي إلى وجود المتشكلين في الحالة الغازية، طاقة جبس الحرة النسبية (ΔG) في كلا المحلولين تساوي (-6.22 and -2.61 Kcal/mol) مما يدل على أن عملية التشكل تصبح تلقائية في كلا المحلولين (at room temperature).

قيمة ثابت الاتزان (K) =(2.76×10^{-5} and 1.22×10^{-2}) في كلا من H_2O and CCl_4 ، في المحلول يكون متشكل الايمينو **NNO$_2$-23ITH** هو المتشكل السائد.

وجود مجموعة (-F) الساحبة للالكترونات في الموضع (٢) يطيل الرابطتين الأحاديتين C_4N_3, C_5S_1 بينما يقلل الرابطة C_4N_6 بحوالي ٠,٠٠٣ Å . أما مجموعة ($-CH_3$) تطيل فقط الرابطة CS مما يدل على إن مشاركة (lone pair) لذرة النيتروجين (N_6) داخل حلقة الثيازول في

(delocalization of the ring) يقل. من ناحية أخرى فان مجموعة ($-CH_3$) تؤثر فقط على طول الرابطة CS حيث أنها تزداد. وجود المشتقات في الموضع (٥) بالنسبة لـ٤-أمينوثيازول له تأثير اقل على الشكل الهندسي مقارنة للمشتق في الموضع (٢) . قيم الطاقة الحرة لجبس (ΔG) و ثابت الاتزان (K) للمشتقات تشير إلى زيادة تركيز نسبة الايمينو أكثر في حالة ٤-أمينوثيازول ماعدا في حالة المشتق **$5CH_3$-4ATH**.

كما أن المذيب ليس له تأثير على الثبات النسبي أو ثابت الاتزان لهذه المشتقات.

٥) ٢-هيدروكسي و٢-ثيو ثيازول

٢-هيدروكسي و٢-ثيو ثيازول توجد في صورة keto and thio بشكل أساسي. ويكون الفرق في الطاقة يساوي (10.94- and -7.24 Kcal/mol) بينما التغيرفي طاقة جيبس الحرة في الوسط الغازي يساوي (10.98- and -2.36 Kcal/mol) و يكون ثابت الاتزان (1.87×10^{-2} و 8.98×10^{-9}) على التوالي.

قيم العزم ثنائي القطب في الوسط الغازي يمكن ترتيبها كالآتي

(0.648 D) **2HTH** < (1.036 D) **2MTH** < (4.431 D) **23OTH** < (5.296 D) **23TTH.**

في المحلول يكون شكلي (keto- and thiothiazoles) هما الأثبت.

REFERENCES

REFERENCES

1- L. Forlani, *Targets Heter. System*, **1**, 75-105 (1997) and references there in.

2- M. Hudlic and A. Pavlath, "*Chemistry of Organic Fluorine compounds II*" A critical Review, *Am. Chem. Soc*., Washington, DC, (1995).

3- J. T. Welch, *Tetrahydron*, **43**, 3123 (1987).

4- P. Crews, Y. Kakou, & E. Quinoa, *J. Am. Chem. Soc*., **110**, 4365-4368 (1988).

5- J. V. Metzeger, "*Comprehensive Heterocyclic Chemistry*", vol. **6**, edited by A. R. Katritzky and C. W. Rees, Part 4B, edited by K. T. Potts, pp. 235-331. Oxford: Pergamon Press., (1984).

6- H. Shinagawa, H. Yamaga, H. Houchigai, Y. Sumita, and M. Sunagawa, *Bioorg. Med. Chem*., **5**, 601-621 (1997).

7- B. Shivarama Holla, K. V. Malini, B. Sooryanarayana Rao, B. K. Sarojini, N. Suchetha Kumari, *Eur. J. Med. Chem*., **38**(3), 313-318 (2003).

8- M. J. S. Dewar, E. G. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc*., **107**, 3902 (1985) .

9- A. M. El-Nahas, *J. Chem. Res*., (S) 222-223 (1998).

10- H. Yekeler and D. Özbakir, J. *Mol. Model*., **7**(4), 103-111(2002).

11- G. Bereket, C. Öğretir, M. Yaman and E. Hür, *J. Mol. Struct*., (*Theochem*), **625**(1-3), 31-38 (2003).

12- A. Maris, P. Ottaviani and W. Caminati, *Chem. Phys. Lett*., **360**(1-2), 155-160 (2002).

13- S. Morpurgo and M. Bossa, *Phys. Chem. Chem. Phys*., **5**(6), 1181-1189 (2003).

14- G. Bakalarski and B. Lesyng, *Pol. J. Chem*., **72**(7, Suppl.), 1792-1797 (1998).

15- P. Ü. Civcir, *J. Mol. Struct*., (*Theochem*), **532**(1-3), 157-169 (2000).

16- S. Millefiori and A. Alparone, *Chem. Phys.*, **303**(1-2), 27-36 (2004).

17- J. G. Contreras, J. B. Alderete, (*Theochem*), **115**(2), 137-141 (1994)

18- P. Ü. Civcir, *J. Phys. Org. Chem.*, **14**(3), 171-179 (2001).

19- A. Broo and A. Holmén, *Chem. Phys.*, **211**(1-3), 147-161(1996).

20- C. Öğretir and M. Yaman, *J. Mol. Struct.*, (*Theochem*), **458**(3), 217-226 (1999).

21- P. Ü. Civcir, *J. Mol. Struct.*, (*Theochem*), **572**, 5 -13 (2001).

22- L. Senthilkumar, P. Kolandaivel, *J. Mol. Struct.*, (*Theochem*), **638**, 69-78 (2003).

23- R. Hilal, Z.M. Zaky and Shabaan A.K. Elroby, *J. Mol. Struct.*, (*Theochem*), **685**, 35-42 (2004).

24- S. Millefiori and A. Alparone, *Chem. Phys.*, **303**, 27-36 (2004).

25- S.X. Tian, C.F. Zhang, Z.J. Zhang, X.J. Chen and K.Z. Xu, *Chem. Phys.*, **242**, 217-225 (1999).

26- M. H. Palmer and D. Christen, *J. Mol. Struct.*, (*Theochem*), **705**, 177-187 (2004).

27- C. Öğretir, T. A. Demir, M. (Özkütük) Yaman, K. Görgün, *J. Mol. Struct.*, (*Theochem*), **679**, 33-34 (2004).

28- H. Yekeler, *J. Mol. Struct.*, (*Theochem*), **713**(1-3), 201-206 (2005).

29- C. Reichardt, *in Solvent and solvent Effects in Organic chemistry*, VCH, Weinheim (1988).

30- J. Elguero, C. Marzin, A. R. Katritzky and P. Linda "*The Tautomerism of Heterocycles*" Academic Press, London, (1976).

31- C. L. Angyl and R. L. Werner, *J. Chem. Soc. Abstr.*, 2911-2915 (1952).

32- Yu. N. Sheinker and E. M. Peresleni, *Zhur. Fiz. Khim.*, **36**, 1705-1712 (1962).

33- J. F. Arenas, J. Perez-Pena, and M. Gonzales-Davila, *Collect. Czech. Chem. Commun.*, **54**(1), 28-41(1989).

34- C. Caranoni and J. P. Reboul, *Acta Cryst.*, **B38**, 1255-1259 (1982).

35- R. Toplak, N. Lan, J. Volmajer, I. Leban and A. M. Le Marēchal, *Acta Cryst.*, **C59**(9), 502-505 (2003).

36- Yu. N. Sheinker, V. V. Kushkin and I. Ya Postovskii, *Zhur. Fiz. Khim.*, **31**, 214-226 (1957).

37- I. T. Depeshko and V. I. Treskach, *Farmatsevtichnii Zhurnal* (Kiev), **6**, 25-28 (1979).

38- L. Forlani, M. Magagni and P. E. Todesco, *Gazz. Chim. Ital.*, **109**(6-7), 377-380 (1979).

39- C. K. Tseng, *Magn. Reson. Chem.*, **25**(2), 105-108 (1987).

40- G. Toth, B. Podanyi, *J. Chem. Soc., Perkin Trans 2*, **1**, 91-94 (1984).

41- R. M. Davidson, J. R. Rice, V. M. Lakshmi, T. V. Zenser and B. B. Davis, *Magn. Reson. Chem.*, **26**(6), 482-487 (1988).

42- L. Forlani, *Gazz. Chim. Ital.*, **111**(5-6), 159-162 (1981).

43- C. D. Gutierrez, V. Bavetsias and E. McDonald, *Tetrahedron Lett.*, **46** (20), 2595-3597 (2005).

44- M. J. Gorczynski, R. M. Leal, S. L. Mooberry, J. H. Bushweller and M. L. Brown, *Bio. Med. Chem.*, **12**(5), 1029-1036 (2004).

45- C. J. Helal, M. A. Sanner, C. B. Cooper, T. Gant, M. Adam, J. C. Lucas, Z. Kang, S. Kupchinsky, Michael'K. Ahlijanian, and B. Tate et al. *Bioorg. Med. Chem. Lett.*, **14**(22), 5521-5525 (2004).

46- R. N. Misra, H. Xiao, D. K. Williams, K. S. Kim, S. Lu, K. A. Keller, J. G. Mulheron, R. Batorsky, J. S. Tokarski, J. S. Sack, S. D. Kimball, F. Y. Lee and K. R. Webster, *Bioorg. Med. Chem. Lett.*, **14**(11), 2973-2977 (2004).

47- A. Vulpetti, E. Casale, F. Roletto, R. Amici, M.Villa and P. Pevarello, *J. Mol. Graphics and Modelling*, **24**(5), 341-348 (2006).

48- A. Göblyös, S. N. Santiago, D. Pietra, T. Mulder-Krieger, J. F. D. Künzed, J. Brussee and A. P. IJzerman, *Bioorg. Med. Chem.*, **13**(6), 2079-2087 (2005).

49- S. Ueda, H. Terauchi, A. Yano, M. Matsumoto, T. Kubo, Y. Kyoya, K. Suzuki, M. Ido and M. Kawasaki, *Bioorg. Med. Chem.*, **12**(15), 4101-4116 (2004).

50- N. J. Datta, R. C. Khunt and A. R. Parikh, Indian *J. Chem., Sect. B*, *Organic Chemistry Including Medicinal Chemistry*, **41B**(2), 433-435 (2002).

51- P. C. Hang and J. F. Honek, *Bioorg. Med. Chem. Lett.*, **15**(5), 1471-1474 (2005).

52- P. Beuchet, M. Varache-Lembège, A. Neveu, J. M. Lèger, J. Vercauteren, S. Larrouture, G. Deffieux and A. Nuhrich, *Eur. J. Med. Chem.*, **34**(9), 773-779 (1999).

53- A. Geronikaki and G. Theophilidis, *Eur. J. Med. Chem.*, **27**(7), 709-716 (1992).

54- C. Papadopoulou, A. Geronikaki and D. Hadjipavlou-Litina, *I1Farmaco*, **60**(11-12), 969-973 (2005).

55- A. Kreutzberger and H. Schimmelpfennig, *Archiv Der Pharmazie*, **314**(5), 385-391 (1981).

56- K. Kralova, D. Loos, F. Sersen and E. Sidoova, *Chemical Papers*, **48**(3), 198-202 (1994).

57- G. Raciti, P. Mazzone, A. Raudino, G. Mazzone and A. Cambria, *Bioorg. Med. Chem.*, **3**(11), 1485-1491 (1995).

58- S. Predhomme, J. P. Demaret, S. Vinogradov, U. Asseline, L. Morin-Allory and P. Vigny, *J. Photochem. Photobiol. B: Biol.*, **53**(1-3), 60-69 (1999).

59- K. A. Karpov, A. V. Nazarenko, B. V. Pekarevskii and V. M. Potekhin, *Ruus. J. Appl. Chem.*, **74**(6), 998-1001 (2001).

60- D. Keil, R. Flaig, A. Schroeder and H. Hartmann, *Dyes and Pigments*, **50**(1), 67-76 (2001).

61- M. A. Metwally, E. Abdel-latif, A. M. Khalil, F. A. Amer and G. Kaupp, *Dyes and Pigments*, **62**(2), 181-195 (2004).

62- K. Singh, S. Singh and J. A. Taylor, *Dyes and Pigments*, **54**(3), 189-200 (2002).

63- M. S. Yen and I. J. Wang, *Dyes and Pigments*, **67**(3), 183-188 (2005).

64- J. Griffiths and W. J. Lee, *Dyes and Pigments*, **57**(2), 107-114 (2003).

65- L. Forlani, M. Sintoni, *J. Chem. Res.,* (*Synopses*), **3**, 110-111 (1986).

66- L.Forlani, M. Magagni and P. E. Todesco, *Chimicae I`Industria* (Milan, Italy), **60**(4), 348 (1978).

67- L. Forlani, P. De Maria, *J. Chem. Soc., Perkin Trans.*2, **5**, 535-537 (1982).

68- L. Forlani, P. De Maria and A. Fini, *J. Chem. Soc., Perkin Trans.*2, **8**, 1156-1158 (1980).

69- J. F Arenas, M. Gonzalez-Davila and J. Perez-Pena, *Optica Puray Aplicada*, **23**(1), 67-72 (1990).

70- G. Costa, *Ann. Chim.*, (Rome, Italy), **43**, 585-601 (1953).

71- J. Perez-Pena, M. Gonzalez-Davila, M. Suarez-Tangil and J. Hernandez-Brito, *Collect. Czech. Chem. Commun.*, **45**(8), 2045-2053 (1989).

72- E. M. Coyanis, C. O. Della Vèdova, A. Haas and M. Winter, *J. Fluorine Chem.*, **117**(2), 185-192 (2002).

73- G. Mill, T. Avignon and J. Chouteau, *Comptes Rendus des Seances de I`Academie des Sciences, Serie B: Sciences Physiques*, **281**(15), 305-308 (1975).

74- H. T. Flakus, A. Miros and P. G. Jones, *Spectrochim. Acta*, **A58**(2), 225-237 (2002).

75- E. S. Stern, *J. Chem. Soc. Abstr.*, 1664-1665 (1949).

76- Yu. N. Sheinker, I. Ya. Postovskii, N. M. Voronina, *Zhur. Fiz. Khim.*, **33**, 302-309 (1959).

77- B. Ellis and P. J. F. Griffiths, *Spectrochim. Acta*, **22**(12), 2005-2032 (1966).

78- L. Bouscasse, M. Chanon, R. Phan-Tan-Luu, J. E. Vincent and J. Metzger, *Bull Soc. Chim. Fr.*, **3**, 1055-1062 (1972).

79- J. L. Garraway, *J. Chem. Soc., Phys. Org.*, **1**, 92-98 (1966).

80- V. Nalini and G. R. Desiraju, *India Acta Cryst., Sec. C: Crystal Struct. Communications*, **C45**(10), 1528-1530 (1989).

81- B. W. Lee and S. D. Lee, *Tetrahedron Lett.*, **41**(20), 3883-3886 (2000).

82- R. Faure, A. Assaf, E. J. Vincent and J. P. Aune, *Journal de Chimie Physique et de Physico-Chimie Biologique*, **75**(7-8), 727-734 (1978).

83- R. Faure, J. P. Galy, E. J. Vincent and J. Elguero, *Can. J. Chem.*, **56**(1), 46-55 (1978).

84- M. Chanon and J. Metzger, *Bull. Soc. Chim. Fr.*, **7**, 2868-2880 (1968).

85- I. W. J. Still, N. Plavac, D. M. McKinnon and M. S. Chauhan, *Can. J. Chem.*, **54**, 1660 (1976).

86- J. Arriau and J. Elguero, *An. Quim. C-Org. Bioq.*, **77**(2), 105-111 (1981).

87- N. N. Kharabaev, V. V. Rachkovskii and A. D. Garnovskii, *Russ. J. Coord. Chem.,* (*Trans. Koord. Khim.,*) **21**(9), 654-657 (1995).

88- G. S. Kapsomenos and P. D. Akrivos, *Can. J. Chem.*, **66**(11), 2835-2838 (1988).

89- J. Fabian and P. Birner, *Wissenschaftliche Zeitschrift der Technischen Universitaet Dresden*, **37**(3), 119-123 (1988).

90- T. Jagodzinski, E. Jagodzinska, T. Dziembowska and B. Szczodrowska, *Khimiya Geterotsiklicheskikh Soedinenii*, **3**, 410-417 (1988).

91- G. Salmona, R. Faure, E. J. Vincent, C. Guimon and G. Pfister-Guillouzo, *J. Mol. Struct.*, **48**(2), 205-217(1978).

92- G. Kapsomenos and P. Akrivos, *Can. J. Chem.*, **64**(11), 2225-2228 (1986).

93- S. Angelova, V. Enchev, N. Markova, P. Denkova and K. Kostova, *J. Mol. Struct.*, (*Theochem*), **711**, 201-207 (2004).

94- D. Tahmassebi, *J. Mol. Struct.*, (*Theochem*), **638**, 11-20 (2003).

95- M. Spassova and V. Enchev, *Chem. Phys.*, **298**, 29-36 (2004).

96- M. H. Plamer and R. H. Findlay, *J. Mol. Struct.*, **40**(2), 191-210 (1977).

97- S. F. Bone, B. A. Smart, H. Gierens, C. A. Morrison, P. T. Brain and D. W. H. Rankin, *Phys. Chem. Chem. Phys.*, **10**, 2421-2426 (1999).

98- L. Marchetti, L. Pentimalli, P. Lazzeretti, L. Schenetti and F. Taddei, *J. Chem. Soc., Perkin Trans. 2*, **14**, 1926-1929 (1973).

99- S. Yarligan, C. Öğretir, I, G. Csizmadia, E. Acikkalp, H. Berber and T. Arslan, *J. Mol. Struct.*, (*Theochem*), **715**(1-3), 199-203 (2005).

100- W. C. Bailey, *J. Mol. Spectrosc.*, **209**(1), 57-59 (2001).

101- G. Crank and H. R. Khan, *J. Heterocycl. Chem.*, **22**(5), 1281-1284 (1985).

102- G. A. Ahmed, *J. Ind. Chem. Soc.*, **72**(8), 525-527 (1995).

103- F. Zuloaga, M. Domard, F. Pautet, H. Fillion and R. Tapia, *Tetrahedron*, **56**(12), 1701-1706 (2000).

104- R. Arnaud, N. Pelloux-Leon, R. Nadia, J. L. Ripoll and Y. Vallee, *J. Chem. Soc., Perkin Trans. 2*, **6**, 1077-1086 (1995).

105- D. Le Gourrièrec, V. A. Kharlanov, R. G. Brown and W. Rettig, *J. Photochem. Photobiol. A: Chem.*, **130**(2-3), 101-111 (2000).

106- P. Purkayastha and N. Chattopadhyay, *Int. J. Mol. Sci.*, **4**, 335-361 (2003).

107- S. El Din H. Etaiw, R. S. Farag, A. M. El-Atrash and A. M. A. Ibrahim, *Spectrochim. Acta*, **48A**(10), 1503 (1992).

108- R. M. Ramadan, A. M. El-Atrash and A. M. A. Ibrahim and S. E. H. Etaiw, *Thermochim. Acta*, **178**, 331-338 (1991).

109- D. E. Lynch, L. J. Nicholls, G. Smith, K. A. Byriel and C. H. L. Kennard, *Acta Cryst.*, **B55**(5), 758-766 (1999).

110- D. E. Lynch, and I. Mc Clenaghan, *Acta Cryst.*, **C60**, 592-594 (2004).

111- V. E. Borisenko, A. Koll, E. E. Kolmakov and A. G. Rjasnyi, *J. Mol. Struct.*, **78**(1-3), 101-115 (2006).

112- G. N. Lipunova, S. L. Mertsalov, N. N. Gulemina, I. Ya. Postovskii and L. G. Egorova, *Zhur. Org. Khim.*, **12**(11), 2460-2464 (1976).

113- B. M. Jordan, E. S. Raper and J. R. Creighton, *Thermochim. Acta*, **62**(1), 21-33 (1983).

114- R. A. Bartsch, Y. M. Chae, S. Ham and D. M. Birney, *J. Am. Chem. Soc.*, **123**(31), 7479-7486 (2001).

115- H. L. Milton, M. V. Wheatley, A. M.Z. Slawin and J. D. Woollins, *Inorg. Chim. Act.*, **358**(5), 1393-1400 (2005).

116- L. M. Nguyen, M. E. Dellinger, J. T. Lee, R. A. Quinlan, A. L. Rheingold and R. D. Pike, *Inorg. Chim. Act.*, **358**(4), 1331-1336 (2005).

117- L. D`Ornelas, T. Castrillo, L. Hernández de B., A. Narayan and R. Atencio, *Inorg. Chim. Act.*, **342**, 1-8 (2003).

118- C. A. Bolos, K. T. Papazisis, A. H. Kortsaris, S. Voyatzi, D. Zambouli and D. A. Kyriakidis, *J. Inorg. Biochem.*, **88**(1), 25-36 (2002).

119- C. Spinu, A. Kriza, L. Spinu, *Acta Chimica Solvenica*, **48**(2), 257-264 (2001).

120- Z. H. Chohan, M. Praveen, *Appl. Organomet. Chem.*, **15**(7), 617-625 (2001).

121- E. Schrdinger, *Ann. Physik.*, **79**, 361 (1926).

122- M. Born and J. R. Oppenheimer, *Ann. Physik.*, **84**, 457 (1927).

123- J. C. Slater, *Phys. Rev.*, **34**, 1293 (1929); **35**, 509 (1930).

124- S. F. Boys, *Proc. Roy. Soc.* (*London*), A **200**, 542 (1950).

125- W. J. Pietro, R. F. Hoult, Jr., E. S. Blurock, W. J. Hehr, D. J. Defrees and R. F. Stewart, *Inorg. Chem.*, **20**, 3650 (1981).

126- M. M. Francle, W. J. Pietro, W. J. Hehr, J. S. Binkley, M. S. Gordon, D. J. Defrees and J. A. Pople, *J. Chem. Phys.*, **77**, 3654 (1982).

127- P. C. Hariharan and J. A. Pople, *Chem. Phys. Lett.*, **66**, 217 (1972).

128- R. Krishnan, M. J. Frish and J. A. Pople, *J. Chem. Phys.*, **72**, 4244 (1980).

129- a) V. Fock, *Z. Physik.*, **61**, 126 (1930).

b) D. R. Hartree, *Proc. Commbridge Phil. Soc.*, **24**, 89 (1928).

130- I. N. Levine, *Quantum Chemistry*, **3**rd Ed., Allyn, and Bacon, Boston, (1983).

131- C. C. J. Roothaan, *Rev. Mod. Phys.*, **23**, 69 (1951).

132- a) C. C. J. Roothaan, *Rev. Mod. Phys.*, **32**, 179 (1960).

b) J. S. Binkley, J. A. Pople and P. A. Dobosh, *Mol. Phys.*, **28**, 1423 (1974).

133- G. G. Hall, *Proc. Roy. Soc.* (*London*), **A 20**, 541 (1951).

134- J. A. Pople and R. K. Nesbet, *J. Chem. Phys.*, **22**, 571 (1954).

135- R. S. Mulliken, *J. Chem. Phys.*, **23**, 1833, 1841, 2338, 2343 (1955).

136- J. A. Pople, J. S. Binkley and R. Seeger, *Int. J. Quantum Chem., Symp.* **10**, 1 (1976).

137- C. Moller and M. S. Plesset, *Phys. Rev.*, **46**, 618 (1934).

138- a) H. A. John and Teller, *Proc. Roy. Soc.*, **A 161**, 220 (1957).

b) R. Renner, *Z. Physik.*, **92**, 172 (1973).

139- J. W. Mclver, Jr., and A. Komorniki, *Chem. Phys. Lett.*, **10**, 303 (1971).

140- E. J. Baerends, D. E. Ellis and P. Ros, *Chem. Phys.*, **2**, 41(1973).

141- A. Rosen and D. E. Eillis, *J. Chem. Phys.*, **65**, 3629 (1976).

142- F. W. Averill and D.E. Ellis, *J. Chem. Phys.*, **59**, 6412 (1973).

143- B. Delley and D. E. Ellis, *J. Chem. Phys.*, **76**, 1949 (1982).

144- B. Delley, *J. Chem. Phys.*, **92**, 508 (1990).

145- R. Car and M. Parrinello, *Phys. Rev. Lett.*, **55**, 2471 (1985).

146- M. P. Teter, M. C. Payne and D. C. Allan, *Phys. Rev.*, **B 40**, 12255 (1989).

147- J. C. Slater, *Phys. Rev.*, **51**, 846 (1937).

148- O. K. Andersen, *Phys. Rev.*, **B 12**, 3060 (1975).

149- E. Wimmer, H. Krakauer, M. Weinert and A. J. Freeman, *Phys. Rev.*, **B 24**, 864 (1981).

150- A. D. Becke, *Int. J. Quantum Chem. Symp.*, **23**, 599 (1989).

151- P. Hohenberg and W. Kohn, *Phys. Rev.*, **B 136**, 864 (1964).

152- W. Kohn, and L. J. Sham, *Phys. Rev.*, **A 140**, 1133 (1965).

153- M. Levy, *Prock. Natl. Acad. Sci.*, (USA) **76**, 6062 (1979).

154- R. G. Parr and W. Yang, "*Density-Functional Theory of Atoms and Molecules*" (Oxford University, New York, 1989).

155- S. H. Vosko, L. Wilk and M. Nusair, *Can. J. Phys.*, **58**, 1200 (1980).

156- H. Sambe and R. H. Felton, *J. Chem. Phys.*, **62**, 1122 (1975).

157- W. J. Hehre, L. Radom, P. Schleyer and J. A. Pople, "*Ab initio Molecular Orbital Theory*" (Wiley, New York, 1986).

158- B. I. Dunlap, J. W. D. Connolly and J. R. Sabin, *J. Chem. Phys.*, **71**, 3396 (1979); **71**, 4993 (1979).

159- B. I. Dunlap, J. Andzelm and J. W. Mintmire, *Phys. Rev.*, **A 42**, 6354 (1990).

160- A. A. Granovsky, http://www. Classic. Chem. msu. su/gran/games/ index. html.

161- M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K.A. Nguyen, S. Su, T. L. Windus, M. Dupuis and J. A. Montgomery, *J. Comput.*, **14**, 1347 (1993).

162- A. D. Becke, *J. Chem. Phys.*, **98**, 5648 (1993).

163- C. Lee, W. Yang and R. G. Parr, *Phys. Rev.*, **B 37**, 785 (1988).

164- S. Miertus and J. Tomasi, *Chem. Phys.*, **65**, 239 (1982).

165- S. Miertus, E. Scrocco and J. Tomasi, *Chem. Phys.*, **55**, 117 (1981).

166- R. Cammi and J. Tomasi, *J. Comput. Chem.*, **16**, 1449 (1995).

167- S. J. Angyal and C. L. Angyal, *J. Chem. Soc. Abstr.*, 1461-1466 (1952).

168- J. V. Metzger, Ed., "*Thiazole and its Derivatives. Part two*."John Wiley & Sons: New York, 1979.

169- J. Dickey, E. Towne and G. Wight, *J. Org. Chem.*, **20** (499) (1955).

170- V. M. Merino and M. J. Gil, *J. Chem. Soc., Perkin Trans. 2*, 801(1999).

171- S. I. Kotelevskii and O. V. Prezhdo, *Tetrahedron*, **57** 5715 (2001).

172- M. K. Cyranski, T. M. Krygowski, A. R. Kartritzky and P. V. R. Schleyer, *J. Org. Chem.*, **67** 1333 (2002).

173- R. M. Ramadan, A. M. El-Atrash and A. M. A. Ibrahim, *Spectrochim. Acta*, **46A**(9), 1305-1312 (1990).

174- S. Angelova, V. Enchev, N. Markova, P. Denkova and K. Kostova, *J. Mol. Struct.*, (*Theochem*), **711**, 201-207 (2004).

175- L. Forlani, A. Medici, P.E. Todesco, Tetrahedron Lett., **17**, 201 (1976).

176- G. J. Kruger and G. Gofner, *Acta Crystallogr.*, **B28**, 272 (1972).

177- E. Spinner, *Spectrochem. Acta*, **A42**(11), 1289 (1986).

178- J. Guillermo and J. B. Alderete, *Chem. Phys. Lett.*, **232**, 61 (1995).

179- C. Cemil and M. Yaman, (*Theochem*), **458**, 217 (1999).

180- K. S. George and A. Pericles, *Can. J. Chem.*, **66**(11), 2835 (1988).